BRAIN

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A Journal of Neurology

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CONTENTS.

	PAGE
Muscle Spindles in Human Extrinsic Eye Muscles. Sybil Cooper and Peter M. Daniel	1
On Amyotonia Congenita. J. W. Aldren Turner	25
Proprioception and the Motor Cortex. E. Gellhorn	35
The Significance of Tinel's Sign in Peripheral Nerve Injuries. J. R. Napier	63
État Marbré of the Thalamus following Birth Injury. R. M. Norman	83
Disorders of the Body Image caused by Lesions of the Right Parietal Lobe. M. Roth	89
Observations on Essential (Heredofamilial) Tremor. Macdonald Critchley	113
Tridione Therapy in Minor Epilepsy. G. R. Davies and J. D. S. Spillane	140
Cerebral Lesions due to Intracranial Aneurysms. E. Graeme Robertson	150
Quantitative Observations on the Olfactory System of the Rabbit. A. C. Allison and R. T. Turner Warwick	186
Experimental "Allergic" Encephalomyelitis. C. E. Lumsden	198
The Orbital Gyri. E. Sachs, Jr., S. J. Brendler and J. F. Fulton	227
Some Observations upon the Otological Effects of Streptomycin Intoxication. M. R. Dix, C. S. Hallpike and M. S. Harrison	241
Hereditary Stenosis of the Aqueductus of Sylvius as a Cause of Congenital Hydrocephalus. D. S. Bickers and R. D. Adams	246
Study of Efferent Connections of the Frontal Lobe in the Human Brain after Leucotomy. M. Meyer	265
The Relative Sympathetic Contribution to Individual Roots of the Brachial Plexus in Man. S. Sutherland and G. M. Bedbrook	297
Adequate Stimuli. J. H. Parsons	302
Sensation and Volition. W. Gooddy	312
Hereditary Ataxia with Optic Atrophy of the Retrobulbar Neuritis Type, with Latent Pallido-Luysian Degeneration. M. André-Van Leeuwen and L. Van Bogaert	340
The Remote Reference of Pain Aroused in the Skin. D. C. Sinclair	364
Progressive Fibrinoid Degeneration of Fibrillary Astrocytes associated with Mental Retardation in a Hydrocephalic Infant. S. Alexander	373
Subacute Combined Degeneration of the Cord. C. C. Ungley	382
The Cross-Sectional Area of Peripheral Nerve Trunks Devoted to Nerve Fibres. S. Sunderland and K. C. Bradley	428
The Spontaneous Electricity of the Human Thalamus. D. Williams and G. Parsons-Smith	450
The Diagnosis of Paraphysial Cysts. J. W. D. Bull and D. Sutton	487
Experimental "Allergic" Encephalomyelitis. II. On the Nature of the Encephalitogenic Agent. C. E. Lumsden	517
The Phenomenon of Tactile Inattention with Special Reference to Parietal Lesions. Macdonald Critchley	538
On Spatial Summation of Sensory Stimuli in Man. J. Droogleever Fortuyn	562
On Thalamic Dysæsthesiæ and their Suppression by Bilateral Stimulation. R. A. Henson	576
Delayed Withdrawal Reflex and Perception of Pain: Studies in a Case of Syphilitic Meningomyelitis and Tabes with Extensor Plantar Responses of a Type Not Previously Described. Michael Ashby	599
The Cross-Sectional Area of Peripheral Nerve Trunks Occupied by the Fibres Representing Individual Muscular and Cutaneous Branches. S. Sunderland and G. M. Bedbrook	613
Notices of Recent Publications	112, 263, 483, 625

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MUSCLE SPINDLES IN HUMAN EXTRINSIC EYE MUSCLES

BY

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INTRODUCTION

THE neuromuscular organs in muscle which were named muscle spindles by Kühne (1863) were shown to be the main proprioceptors of the skeletal muscles of the body by Sherrington (1894–95). The fact that these organs are absent in the extrinsic eye muscles of certain species of animals has led to the widespread belief that they are absent from the eye muscles of all species, including man. Although Sherrington (1918) showed by simple experiments and clear argument that the basis of ocular, as of other, posture must depend on a proprioceptive function of the extrinsic ocular muscles, and though there is evidence that other types of sensory endings are present in the eye muscles of all animals, many modern writers contend that eye muscles have no proprioceptive innervation and furthermore that, on theoretical grounds, there is no need for proprioceptors in these muscles (Irvine and Ludvigh, 1936; McIntyre, 1941; Morson, 1941; Adler, 1945; Cogan, 1948).

In the course of earlier work by one of us on the extrinsic muscles of the human eye (Daniel, 1946) it was noted that in certain transverse sections there were groups of muscle fibres, associated together and enclosed within a connective tissue capsule, which had the appearance of small muscle spindles. We decided to investigate these structures further and quickly realized that they were quite frequent in certain parts of the muscle but were completely absent in the mid-part of the muscle belly, the region that is usually examined. We have found that they are indeed muscle spindles, though they differ in points of detail from the muscle spindles of other somatic muscles. The purpose of this paper is to describe these organs in the extrinsic eye muscles of man, to show the sites at which they are found and to discuss their significance. A comparison is also made between the muscle spindles of eye muscles and those of

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lumbrical muscles, and the presence of spindles in the eye muscles of certain animals is mentioned.

Muscle spindles are widely distributed, being particularly numerous in some of the postural muscles of the limbs (Gregor, 1904) and especially in those muscles of the extremities that are used to carry out fine movements (Voss, 1937). It has long been something of a puzzle that they are considered to be absent from the extrinsic muscles of the eye, muscles which are very delicately adjusted to all changes of posture and which in man, at least, are capable of extremely fine movements. Sherrington (1897) did not find muscle spindles in the eye muscles of the macaque monkey, the cat or the rabbit, though later Tozer and he (1910) described many tendon organs in the eye muscles of these animals. Crevatin (1900) recorded spindles in the eye muscles of the ox. Dogiel (1906*a*, 1906*b*) found tendon organs in the eye muscles of man, monkey, ox, horse, dog and cat, and he also found muscle spindles in those of the ox. Cilimbaris (1910) gave a detailed account of muscle spindles in the eye muscles of the sheep, and mentioned their presence in the eye muscles of ox, deer, goat and wild pig and their absence in those of the domestic pig, horse, cat, dog, fox, rabbit, hare and rat. Wohlfart (1935) reported numerous muscle spindles in the eye muscles of calves. Sutton (1915) described structures which he claimed to be muscle spindles in the eye muscles of the embryo pig, but he maintained that certain details of their nervous structure were not found after birth. Woollard (1931) and Hines (1931) found no spindles in the eye muscles of rabbits. The former worker looked at some eye muscle from one human case, but saw no muscle spindles. His search did not appear to be very extensive so that he presumably missed those regions of the muscle in which spindles are present. Pallot (1934) saw simple spiral nerve endings in the eye muscles of the cat, but they were associated with one muscle fibre only, and were not encapsulated.

This short survey suggests that the innervation of the extrinsic eye muscles differs greatly in man and different animals and that further study is needed to determine the varieties of complicated nerve endings, including proved sensory endings, present in the different orders.

The structure and sensory nature of mammalian muscle spindles was originally worked out in detail by Sherrington (1894–95) and Ruffini (1893, 1897, 1898) and an account of the human muscle spindle with a valuable historical survey is given by Batten (1897). In this paper Batten says that he was unable to find spindles in the muscles of the eye, but that his search was by no means exhaustive. Many later accounts of muscle spindles have appeared among which may be mentioned those of Sherrington (1900), Pick (1900), Elwyn (1929), Hines (1930), Creed, Denny-Brown, Eccles, Liddell and Sherrington (1932) and Hinsey (1934). Barker

(1948) has made a new study of the innervation of skeletal muscle spindles in the rabbit.

A detailed description of the gross anatomy of the human extrinsic eye muscles is given by Whitnall (1932) and comparative studies may be found in Ovio (1925) and Walls (1942). We need only point out here that the six extrinsic eye muscles of man are long (all about 4 cm.) and delicate. The recti are inserted well anterior to the equator of the globe, whilst the obliques are inserted near the equator. They are thus capable of bringing about big movements of the eyeball and making all those adjustments called for in binocular and stereoscopic vision, and associated with upright posture and the emancipation of the fore-limbs.

In animals the range of eye movement varies greatly in the different species, and the gross and microscopic anatomy of the extrinsic eye muscles varies accordingly.

Reviews of the histological characteristics of eye muscles of various animals are given by Hinsey (1934), Irvine (1936), and Lauber (1936). These muscles are composed of parallel cross-striated muscle fibres and according to Lockhart and Brandt (1938) all the fibres in human eye muscles run the full length of the muscle. The muscle fibres are small in diameter compared with those of other somatic muscles but may vary greatly between limits of about 10 to 50 μ across (Wohlfart, 1935; Voss, 1935). Woollard's (1931) discussion of muscle fibre size referred only to the rabbit.

Schiefferdecker (1904) described the large amount of connective tissue lying between the muscle fibres in eye muscle, giving sections of these muscles a charactistic appearance. He said that much of it is made up of elastic fibres and that the function of these is to bring a muscle back to its resting length after a contraction of its antagonist. This mechanism has been assumed by some to take the place of a stretch reflex initiated by proprioceptors. The considerable quantity of connective tissue around the muscle fibres of eye muscles is one of the factors which has prevented the recognition of the capsules of muscle spindles, since amidst so much connective tissue a thin capsule is not prominent.

In the case of all the human extrinsic eye muscles the nerve enters the muscle at approximately the junction of its posterior and middle thirds and divides up at once into branches (Frohse, 1898) of which many run distally, whilst numbers bend round to run towards the origin of the muscle. The very great number of nerve fibres seen in the extrinsic eye muscles has been commented on by all observers.

Stibbe (1929) has pointed out that in the human fœtus the 6th cranial nerve is as big as the inferior gluteal nerve, although the gluteus maximus is seventy-four times as heavy as the lateral rectus oculi. Whitnall

(1932) observed that the 6th cranial nerve is, relative to its muscle, the largest nerve in the human body.

Estimates of the relative numbers of nerve fibres to muscle fibres in eye muscles have been made by Tergast (1873) in the sheep, and by Bors (1925–26) in man. These authors give a strikingly high ratio of nerve fibres to muscle fibres, compared with limb muscles. No deductions as to the relative number of motor or sensory nerve fibres can be made from these findings, but they indicate a very small motor unit, even though we now know that the oculomotor nerves have a considerable sensory component. Sherrington (1894–95) showed that the sensory component in nerves to limb muscles was of the order of a third to a half of the total number of nerve fibres, but there is unfortunately no method at present for making a comparable study in nerves to eye muscles.

Physiological aspects of the eye muscles were studied by Sherrington (1893) who obtained reflex responses on stretching the inferior oblique muscles of the cat and macaque monkey (*see infra*, p. 14). Later workers were less successful in obtaining physiological evidence of sensory innervation of the eye muscles (Maré, 1928: McCouch and Adler, 1932: Corbin and Harrison, 1940; McIntyre, 1941).

Some evidence of sensory innervation of the extrinsic eye muscles comes from ophthalmic surgeons who report that undue manipulation of the muscles may induce nausea in the patient. Abd-el-Malek (1938) also described how stimulation of the central ends of the 3rd, 4th and 6th cranial nerves in the cat led to a definite rise in blood-pressure. The tone of the eye muscles, which helps to maintain the intra-ocular pressure (Colle, Duke-Elder and Duke-Elder, 1931) appears to be similar to the postural tone of the limb muscles which is dependent on the intact proprioceptive supply of the muscles.

Working with Dr. D. Whitteridge we have obtained unequivocal evidence of sensory impulses, originating in the extrinsic eye muscles of goats. We have recorded these electrically (Cooper, Daniel and Whitteridge, *J. Physiol.*, in the press).

Materials and Methods Used

The muscles on which this study is based were obtained from about 60 patients who had shown no evidence of ocular palsy or of muscular or neuromuscular disease during life, and whose ages varied from new-born to 82 years.

The orbital contents were taken out at necropsy, as soon after death as possible, usually within twenty-four hours, sometimes within three or four hours, since the occurrence of autolysis in ocular muscles is of great importance. It leads to some disintegration of the connective tissue which makes identification of the thin capsules of the muscle spindles difficult. The individual extrinsic eye muscles were dissected

out, pinned out on cork and fixed in 10 per cent formal-saline, or the whole muscle cone was fixed and the individual muscles dissected out after fixation. Great care was taken in dissecting the origins of the muscles from the bone as the proximal third of the muscle proved of most interest in our work. At the insertions a small block of sclera was left attached to the tendons (except in the case of the superior oblique whose tendon was usually cut at the level of the trochlea).

After fixation, various methods were adopted. For the preparation of routine series of transverse sections a muscle was dehydrated and impregnated with paraffin, then removed from the hot paraffin, and carefully flattened as it cooled. It was cut transversely with a sharp knife into segments about 3 to 4 mm. thick. Each segment of muscle was turned on to its proximal cut edge and the series of segments re-embedded, in order, in paraffin. This provided a single large paraffin block with 8 to 10 adjacent segments in it. When this block was cut it gave a big "section" which was mounted as a whole on one slide, to give 8 to 10 transverse sections taken from 8 to 10 successive parts of the muscle. The resulting slide had the appearance of the diagram in fig. 1B. Some blocks prepared in this way and containing 8 to 10 segments of muscle were sectioned serially right through, so that the total number of muscle spindles present in a particular muscle could be counted and their exact distribution throughout the muscle ascertained.

Large numbers of these blocks containing 8 to 10 segments of muscle were made and from those that were not sectioned serially throughout, a number of successive sections were cut and stained by different methods. In this way details of muscle spindle structure were studied. Also, by means of short runs of serial sections, the total length of many muscle spindles was calculated. Records of the structure and sites of these muscle spindles were made with the aid of a camera lucida.

Not all transverse sections of muscles were prepared in this segmental way and in some instances a single transverse segment was used.

The sections from all these paraffin blocks were cut at from 7 to 30 μ, depending on which staining method was used.

Many muscles embedded in paraffin were cut longitudinally, also at 7 to 30 μ, and stained by different methods.

Other muscles were embedded in celloidin. Transverse and longitudinal sections were cut from these blocks, usually at 15 or 30 μ, but occasionally as thick as 80 μ.

Great numbers of frozen sections were cut from eye muscles, mainly longitudinal, but sometimes transverse, at thicknesses varying from 15 to 80 μ. These sections were used for the study of nerve fibres by silver impregnation methods, as were the thick celloidin sections.

In preparing eye muscles for longitudinal sections, either with paraffin or celloidin embedded material, or with frozen sections, great care was necessary to have the muscles as flat as possible and to make the cuts parallel to the muscle fibres. Identification of muscle spindles in human extrinsic eye muscles is extremely difficult in longitudinal sections if the muscle is slightly twisted or if it is obliquely cut.

The routine stains used for the paraffin and celloidin sections were Ehrlich's hæmatoxylin and eosin, and Weigert's iron hæmatoxylin and van Gieson's mixture. These methods were amplified by Masson's trichrome stain (using anilin blue or light green), Mallory's phosphotungstic-acid hæmatoxylin method, and frequently by Holmes' (1947) "silver on the slide" method, often counterstained by van Gieson's mixture or by Masson's trichrome stain. Hart's modification of Weigert's fuchselin and neutral red method was used for the demonstration of elastic fibres. The Weigert-Pal method was also used with selected muscles for the demonstration of myelin sheaths.

We found it a valuable line of approach to use different stains on successive

sections as one stain so often clarified or corroborated the picture seen in the next section.

The frozen sections were usually stained by one or other of the modifications of the Gros-Bielschowsky method, sometimes counterstained with van Gieson's mixture or light green or anilin blue. The Gros-Bielschowsky method was also used on celloidin embedded material.

We have examined the extrinsic eye muscles from various animals and this material has been prepared in a similar manner.

Results

The form and size of the muscle spindles. – We first identified muscle spindles in extrinsic eye muscles in transverse sections. The muscle spindles were traced in successive sections stained by different methods and the various parts of their structure were compared. Sometimes the whole length of a spindle was traced through serial transverse sections and careful drawings were made of the organ at each stage so as to build up a composite picture. Further information was gained by the more difficult study of longitudinal sections.

From these studies it became clear that the muscle spindle found in the extrinsic eye muscles of man is a smaller and more delicate end-organ than the comparable structure in the other somatic muscles. Like its larger counterpart it consists of a group of fine cross-striated muscle fibres, with a rich nerve supply, enclosed in a torpedo-shaped capsule of fibrous tissue.

The capsule is thin, consisting of two, or at most three, laminæ of fibrous tissue, with characteristic flattened nuclei (fig. 6), and it is continuous from end to end of the spindle. It appears particularly well defined in young subjects (fig. 7). The muscle fibres within the capsule, the intrafusal fibres, are of small diameter, generally about 7 to 20 μ (figs. 6 and 7). Usually they are a little smaller than the surrounding extrafusal fibres, sometimes of the same size; an occasional fibre is larger (fig. 4). Their number is usually two, three or four, but we have found up to ten and as few as one (fig. 15) in one spindle. These intrafusal fibres usually run from pole to pole of the spindle. They may end at the termination of the capsule by joining the fibrous tissue, or more often they pass out of the capsule and become indistinguishable from the extrafusal fibres amongst which they now lie. Sometimes an intrafusal fibre is seen to pass out through the capsule before it reaches the end of the spindle. We have not seen an intrafusal muscle fibre splitting into two daughter fibres; nor have we seen "Ringbinden" (*see infra*, p. 14) around one of these fibres in a human muscle spindle, even though many may be present around extrafusal fibres in old subjects. One was noted around an intrafusal fibre in a rectus oculi of a 20-year-old giraffe.

The intrafusal muscle fibres are rich in nuclei, especially in the equa-

torial region of the muscle spindle. Many of these nuclei are centrally instead of peripherally placed (figs. 6, 7, and 14), and sometimes in a transverse section two or three nuclei may be seen lying together in the interior of an intrafusal fibre. The striking group of rather vesicular nuclei, which appear almost to replace the intrafusal muscle fibre in the equatorial region in other somatic muscle spindles, are not so obvious in the intrafusal fibres of human eye muscle spindles.

The relationship of the capsule to the intrafusal muscle fibres varies considerably at different levels in the length of the spindle. In the equatorial zone the capsule forms a very clear cut ring round the intrafusal muscle fibres, and here the periaxial space is widest (figs. 6 and 7). Muscle spindles are thus most easily recognized in sections which happen to cut them in this region. This periaxial space is most noticeable in paraffin sections and much less marked in celloidin or frozen sections, which suggests that it is at least in part an artefact. It may be of no great size in life. It is crossed by a few tenous fibrils of connective tissue, though there is little connective tissue around the intrafusal fibres in the equatorial zone. Towards the poles of the spindle (figs. 2 and 3) the capsule sends in many stout bands or septa which encircle and bind together the individual intrafusal muscle fibres, thus giving a very different picture from that seen in the equatorial zone. At the poles also the capsule invests the intrafusal fibres more closely, and no periaxial space is seen, even in paraffin sections. Frequently the connective tissue also extends to include several of the neighbouring extrafusal muscle fibres, as in fig. 3. Small blood vessels are also seen in the spindles (figs. 6 and 8).

A typical muscle spindle is always approached by a small nerve trunk (figs. 8 and 9) which is usually incorporated in the capsule at some point (fig. 11). Nerve fibres from this small trunk enter the spindle at various places along its length. Some of these nerve fibres run spirally between the laminæ of the capsular wall (fig. 11). Often a myelinated nerve fibre inside the capsule is seen to encircle the whole group of intrafusal muscle fibres. Both myelinated and non-myelinated nerve fibres have been seen encircling individual intrafusal muscle fibres. Other nerve fibres, after passing through the capsular wall, ramify amongst the intrafusal muscle fibres making a pattern which is far from clear. At the poles of the spindles, where connective tissue septa separate the intrafusal muscle fibres from each other, there is another complex pattern of nerve fibres.

We have not completed our study of the nerve pattern within the muscle spindles, and hope to give more details in a later paper.

Longitudinal sections confirm this description of the structure of the muscle spindle. The muscle spindles are often obscured by an overlying nerve trunk and there is the further difficulty of getting enough of a

spindle in the plane of one section. Fig. 8 shows an almost complete muscle spindle, whilst fig. 9 gives the more usual finding of only part of a spindle.

The muscle spindles of human extrinsic eye muscles vary greatly in length, the shortest being about 50 μ and the longest over 1 mm. long. Many are about 500 μ in length and few are longer than 1 mm. The length of the spindles does not seem to bear any relation to the number of intrafusal muscle fibres found in them. In diameter the spindles vary from 20 to 100 μ, the majority of them being between 40 and 80 μ across.

Distribution of the muscle spindles. – The distribution of muscle spindles in extrinsic eye muscles can only be worked out satisfactorily by the study of transverse sections. In some zones of the muscles the spindles are absent, whilst in others they are abundant. A transverse section through one of the zones of an inferior rectus oculi muscle in which muscle spindles abound is shown in fig. 12. In this field three spindles are very clearly seen whilst the fourth is a polar cross section and is not nearly so striking. Fig. 13 is a comparable cross section from the same block but from further along the length of the muscle. Three of the spindles present in fig. 12 are still seen, but the fourth (the one at the top right-hand corner of fig. 12) is no longer seen, having ended before the plane in which this section was taken.

In the middle third of the extrinsic eye muscles, the zone which is particularly rich in nerve trunks and various types of nerve endings, no muscle spindles are found, whilst both proximal and distal to this region spindles are present. As we became familiar with this distribution of the muscle spindles, which is seen in all the extrinsic eye muscles, it became very much clearer to us why the spindles had formerly been missed in human material.

A block cut from an eye muscle at random is of little use for any detailed survey of the muscle spindle distribution and we developed the technique of preparing a whole muscle in eight to ten segments as described above. This gave us slides with specimen transverse sections taken at roughly 4 mm. intervals throughout the muscle. Fig. 1B shows diagrammatically the appearance of such a slide. The nine sections shown in this figure were taken from a human inferior rectus oculi muscle.

A microscopical study of these sections makes it clear that the internal organization of ocular muscles is very different from that seen in other somatic muscles. The muscle spindles are present only in specific areas of the muscle and the extrafusal muscle fibres themselves show a characteristic pattern in different parts of the muscle, as do the nerve trunks and fibres. The connective tissue lying between and around individual muscle fibres, and much denser than its counterpart in other somatic muscles, is

more abundant in some parts of the muscle than in others. A knowledge of all these varying appearances enables one to recognize the approximate region of the muscle from which any section is taken.

The abundance of connective tissue between individual muscle fibres and the profusion of nerve fibres seen in these muscles make identification of muscle spindles most difficult, as their delicate capsules are obscured and their complement of nerve fibres is little greater than that of extrafusal parts of the muscle.

In the proximal part of the inferior rectus muscle (fig. 1B, Segments 1 and 2) the main nerve trunks are still exterior to the muscle though there are numerous recurrent small nerve trunks, often associated with muscle spindles or going to end-organs at the musculo-tendinous junction (fig. 16). The majority of extrafusal muscle fibres in this region are of uniform and rather small diameter, being of much the same diameter as the intrafusal muscle fibres. The smallest extrafusal fibres seen here are about 10 μ in diameter. There are, however, a few large extrafusal muscle fibres, having diameters of up to 50 μ, and presenting a striking picture when seen in a field of medium-sized fibres (fig. 2). These large fibres often have nerve fibres associated with them in a fairly elaborate pattern.

In the region of the junction of posterior and middle thirds of the muscle the main nerve trunks are entering and here numerous muscle spindles are seen to be lying around the periphery of the muscle, a short way in from the surface. The muscle fibres in this peripheral zone are again mainly of small diameter, whilst the central fibres appear to be increasing in diameter.

Just anterior to this region, in the mid-zone of the muscle, the main nerve branches break up into smaller trunks (fig. 19). Here the majority of the muscle fibres are large in diameter, up to 25 to 30 μ in children and 30 or 40 μ in adults. Many typical motor nerve endings are found here, but *no muscle spindles are seen.* Distal to this, but still in the middle third of the muscle the nerve trunks are still more divided, so that there is a very high proportion of nerve fibres to muscle fibres. Here many nerve fibres encircle large muscle fibres to form the simple spiral endings (figs. 17, 18). These spiral nerve endings may well be sensory and are possibly a modified form of the annulo-spiral ending seen in muscle spindles, though they have no capsules or other characteristics typical of muscle spindles. We have never seen true encapsulated muscle spindles in this region of ocular muscles. The peripheral layer of smaller muscle fibres is entirely absent here and only begins again (distally) as the dense fringe of nerve fibres and spiral endings finishes.

As the distal third of the muscle is reached the extrafusal muscle fibres become smaller in diameter again and take on the appearance of those

seen in the proximal third of the muscle. Muscle spindles, often of rather large size, are found. The muscle here differs in appearance from its more proximal part in having larger numbers of small blood-vessels running in it. These are partly vessels supplying the muscle itself, but many are arteries which traverse the muscle to become the anterior ciliary arteries.

As the muscle approaches its insertion the outer sheath and the inner connective tissue thicken and may contain much elastic tissue. The muscle becomes tendinous and tendon organs are present, but no muscle spindles are seen.

It is thus possible to identify the region of an eye muscle from which a transverse section has been taken and to predict the distribution of muscle spindles in that neighbourhood. This becomes of importance in studying longitudinal sections for it makes it unnecessary to search in the dense band of nerve fibres, in the middle third of the muscles (fig. 10), for muscle spindles and stresses the value of searching in the proximal and distal areas adjacent to the central band. An interesting feature of eye muscles is the variation in diameter of the extrafusal muscle fibres as they pass along the muscle. In cross section all the muscle fibres have a rounded outline.

The structural arrangement of all the extrinsic eye muscles is essentially similar and the muscle spindles are always absent from the rich band of nerve fibres in the belly of the muscle. Levator palpabræ superioris was also examined: it has muscle fibres of more uniform diameter, less connective tissue and far fewer nerve trunks than are found in the other six muscles. A few muscle spindles are present.

In order to get more exact information about the total number and distribution of the muscle spindles an inferior rectus oculi muscle was taken and cut into nine segments. These were embedded together and cut serially at 20 μ and the nine sections on every fifth slide were examined. The segment outlines were drawn by the aid of a camera lucida and the site and slide number of the cross sections of every muscle spindle seen were entered on these outlines. Simplified drawings of these results are given in fig. 1B. A small number of muscle spindles, of less than 80 μ in length, were certainly missed by this method, but other measurements have shown that relatively few muscle spindles in extrinsic eye muscles have a length of under 100 μ. From this work it was possible to construct the completed diagram shown as fig. 1B in which the solid black dots represent all the muscle spindles of over 80 μ in length found in each segment. Since the approximate length of each muscle spindle could be calculated by this method, it was further possible to construct fig. 1A. On the longitudinal outline of the muscle all the muscle spindles were entered in one plane and each spindle was drawn to scale in length. The original

drawings identify each muscle spindle in fig. 1 A and B by number, but in the present small scale reproduction these numbers have had to be omitted.

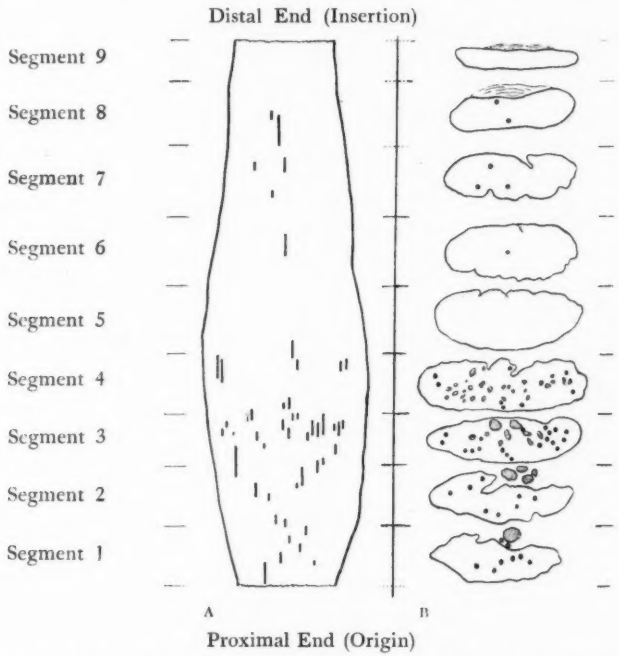

FIG. 1.—A. Outline drawing of the full length of a human inferior rectus oculi muscle. The short black lines represent, in one plane, all the muscle spindles found in this particular muscle. These lines are drawn accurately to scale in length and represent the lengths of the individual muscle spindles relative to each other.

B. The inferior rectus muscle shown in fig. 1A was cut transversely into nine segments, which were turned on end so that transverse sections could be cut. The outlines of each of the nine segments are shown here. Within the outline of each segment *all* the muscle spindles found in that segment are shown as solid black dots. The total number of spindles was found by means of serial sections through the whole segment. The cross-hatched areas are nerve trunks. In Segments 8 and 9 the tendon of insertion is seen replacing the upper aspect of the muscle.

By comparing the spindles seen in any segment of A with the corresponding segment seen in transverse section in B the site of an individual muscle spindle within the muscle can be found. Thus in fig. 1A in Segment 4 two spindles can be seen towards the right of the muscle. These appear to be very close together, but reference to Segment 4 of fig. 1B shows that they are separated from one another by some distance.

In this inferior rectus oculi muscle the greatest number of muscle spindles is found in the proximal part, and none at all are found in the mid-region (Segment 5).

The distribution of muscle spindles in this particular muscle is illustrated in fig. 1B. Forty-seven muscle spindles in all were counted,

forty-one in the proximal third and six in the more distal region of the muscle. Segment 3 was the richest in muscle spindles, having nineteen. Segments 5 and 9 contained no muscle spindles. The single spindle in Segment 6 was situated distal to the fringe of simple spiral endings. The muscle spindles found varied in length between about 120 and 1,640 μ. Twenty-five of them were between 200 and 400 μ, and sixteen between 400 and 1,000 μ long. Five of them were over 1 mm. in length.

Detailed counts were not made of the muscle spindles of the other extrinsic eye muscles, though the numbers were roughly estimated. The inferior recti oculi always appeared to contain the greatest number of spindles though all the recti were richly supplied. The obliques seemed to have a rather smaller complement than the recti. The levator palpebræ superioris is always poorly supplied with spindles.

Comparison of eye muscle spindles with muscle spindles of lumbrical muscles of the human hand.—For comparison with the extrinsic eye muscles, the distribution and number of muscle spindles in the first lumbrical muscle of the human hand was studied. This muscle is about the same length as a rectus oculi muscle. It has small parallel muscle fibres and is richly supplied with muscle spindles. Lumbrical muscles were cut into segments which were embedded in one paraffin block so that a series of transverse sections were obtained, similar to those used for studying the eye muscles and illustrated in fig. 1B. One of these large blocks was cut serially into 15 μ sections and every tenth section was used for counting the spindles.

The lumbricals illustrate well many of the differences between other somatic muscles and eye muscles. The muscle fibres are arranged in compact bundles, and each fibre in cross section is usually polygonal, as Bowman (1840) observed when studying fresh muscles. The connective tissue is sparse between the individual muscle fibres, but it forms thick septa between the muscle bundles and is rich in elastic tissue. It is hard to say how the relative total amounts of elastic tissue compare in the lumbricals and the recti oculi.

The muscle spindles in the first lumbrical muscle are usually situated in the connective tissue septa between muscle bundles, in close relation with nerve trunks and the larger blood-vessels. They are present throughout the muscle, being most numerous in the belly. They are very striking owing to the thickness of their capsules. There may be ten or more laminæ forming the wall of the capsule (fig. 20), suggesting in cross sections a relationship with Pacinian corpuscles. The intrafusal muscle fibres and internal arrangement of the spindles follow the classical descriptions of human spindles (Christomanos and Strössner, 1891; Forster, 1894; Batten, 1897), except that no intrafusal muscle fibres were seen to split

into daughter fibres. The collection of lightly stained nuclei in the intrafusal muscle fibres, in the equatorial region of the spindle, is very marked, and in certain longitudinal sections the intrafusal muscle fibres give the appearance of splitting and then joining up again beyond these nuclei. In transverse sections these nuclei can be seen within a thin ring of muscular tissue.

The larger nerve trunks in the muscle are mostly associated with the muscle spindles. Apart from a restricted area of motor endings, the rest of the muscle shows few nerve fibres. There are isolated trunks going to supply muscle spindles and tendon organs, and there are some nerve fibres of very small diameter. The general picture thus offers a striking contrast to the eye muscles with their rich and widely distributed complement of nerve fibres.

The total number of muscle spindles found in a human first lumbrical muscle examined by the method of serial transverse sections was forty-nine; this agrees well with the totals of forty-seven, forty-nine, fifty-nine and fifty-one muscle spindles found in human first lumbrical muscles by Voss (1935).

Muscle spindles in the eye muscles of other animals.—The method of studying a series of adjacent segments of an eye muscle in routine transverse sections has been used with all the animal eye muscles that we have examined. Up to the present we have found muscle spindles in the extrinsic eye muscles of the cow, white tailed gnu, goat, wild and domestic sheep, pig, giraffe, and in those of the chimpanzee.

We found that the eye muscles of the sheep and goat were very well provided with muscle spindles. The domestic pig, also, undoubtedly has muscle spindles, though Cilimbaris (1910) appears to have missed them. The general structure of the eye muscles of the chimpanzee and the distribution of the muscle spindles much resembles the pattern seen in man.

We have found no muscle spindles in the extrinsic eye muscles of the rabbit, cheetah, cat, dog, bear or macaque money. A poorly fixed specimen of a gibbon's eye muscle gave inconclusive results, but the large number of nerve fibres seen in it was striking. The number of nerve fibres and nerve endings varied greatly in the eye muscles of the different animals, being relatively small in the rabbit as compared with the monkey; but in every eye muscle examined there are far more nerve fibres than are ever seen in any other somatic muscle.

In the extrinsic eye muscles of macaque monkeys tendon endings are numerous. In the eye muscles of the cat we have seen examples of nerve fibres encircling single muscle fibres in the anterior part of the middle third of a rectus muscle. These are probably the non-encapsulated simple

spirals of Pallot (1934) and may be similar to the simple spiral nerve endings in man described by one of us (Daniel, 1946).

"Ringbinden," the bands or rings of cross-striated muscle fibre, which may be seen encircling longitudinal muscle fibres, are frequently mentioned in the literature as being present in the extrinsic eye muscles. We have seen them often in the eye muscles of man and animals, and agree with Wohlfart (1932, 1938) that they are a product of age.

Discussion

The movements of the eyes are frequently mentioned as an example of extremely delicate reciprocal innervation. The posture of the eyeballs is exquisitely adapted to maintain the visual field, and all movements of the eyes are carried out with full reflex co-ordination. Many of the stimuli causing this activity are derived from regions that are remote from the eye muscles (e.g. those from the retina, cerebral cortex, labyrinths, neck muscles, &c.). But detailed work on the limb muscles has shown how dependent the finer adjustments of any somatic muscle are on the intact proprioceptive supply of the muscle itself (Sherrington 1906*a*, 1906*b*, 1915, 1924). Impulses from an active limb muscle also reinforce to an appropriate degree the synergists and inhibit equally delicately the antagonists (Cooper and Creed, 1927*a*, 1927*b*). That such finer adjustments due to the muscles' own proprioceptors are equally necessary for the activities of the eye muscles has been widely accepted. Owing, however, to the difficulties of investigating the innervation of these muscles a school of thought is gaining ground which holds that they have no proprioceptive supply. The study of the nerve endings in other somatic muscles is simplified by the presence of separate sensory and motor spinal nerve roots and experimentally it is possible to identify the sensory endings when the motor supply has degenerated after section of the motor roots. The 3rd, 4th and 6th cranial nerves have no such separate motor and sensory divisions on their course to the brain-stem and whilst it is clear that the motor cells are situated in the nuclei of origin of the appropriate nerve, the site of the sensory nerve cells is still a subject of controversy (Tarkhan, 1934; Corbin and Oliver, 1942). Thus other methods must be used to study the function of the nerve endings in the extrinsic eye muscles. But the absence of a separate sensory path and lack of knowledge of the central connexions does not imply the absence of sensory endings.

In an early experiment Sherrington (1893, p. 410) described how he applied a delicate stretch to the detached global end of the inferior oblique muscle of the cat or macaque monkey and he writes: "Reflex actions were in this way easily obtained, but were inconstant in character; the eyeballs were generally moved, perhaps most frequently conjugately, toward the

side corresponding to the stretched muscle. . . . Sometimes the reflex obtained did not affect the eyes at all; the movement was often a pricking of the ear, either with movement of the eyes or apart from the eye movement." He abolished these reflexes by section of the inferior oblique division of the 3rd nerve.

The further investigation of this reflex depends, in part, on a histological investigation of the nerve endings in the extrinsic eye muscles, especially those endings which differ from characteristic motor endings. Many of the endings described by Marchi (1882), Ciaccio (1891), Retzius (1892), Huber (1899, 1900), Crevatin (1900, 1902) Levinsohn (1902), Dogiel (1906*a*, 1906*b*), Tozer and Sherrington (1910), Hines (1931), Pallot (1934), Daniel (1946) and others cannot be described as typical motor endings, and some of these endings undoubtedly have a sensory function. If, now, structures or endings can be found in the extrinsic eye muscles, of a type that is known to be sensory in other somatic muscles, then it is reasonable to suppose that such endings are also sensory in the eye muscles. Apart from tendon organs, the muscle spindles are the proved proprioceptive organs of other somatic muscles. Earlier workers have shown that muscle spindles exist in the eye muscles of certain animals and we have extended the work to human material and have shown that they are present in considerable numbers in all the human extrinsic eye muscles. Other structures and nerve endings whose function must be sensory are also present so that, while claiming for the spindles a share in the proprioceptive supply of these muscles, we would not claim for them the whole or major share. Indeed the fact that Sherrington obtained reflex responses from the eye muscles of the cat and monkey, although in these animals the muscles are devoid of muscle spindles, shows clearly that there must be other sensory endings in them. The numerous endings in the tendons of the eye muscles prove that there is a rich afferent supply from these parts.

The muscle spindles that we have found in the extrinsic eye muscles do not resemble in every detail the muscle spindles of the other adult human somatic muscles though the general pattern is essentially similar. The most striking difference is the very much thinner capsule in the eye muscle spindles. Little has been written about the thickness of capsules but from our own studies we have gained the impression that they tend to be thickest in the large muscle spindles of such muscles as the lumbricals which are in an exposed position, and are thinner when the spindles are deep in the belly of a limb muscle or are in well-protected muscles such as the erector spinæ. If the muscle spindle capsule is partly protective in nature then structures in the eye muscles in the bony orbit would be in small need of such protection. If its function is to act as part

of the recording mechanism, then its thinness would suggest that it had to deal with very delicate stimuli in eye muscles.

The intrafusal muscle fibres in the muscle spindles of limb muscles are strikingly smaller in diameter than the extrafusal, whereas in eye muscles the difference in diameter between the two types of muscle fibre is much less obvious, owing to the smaller size of the extrafusal fibres.

The sensory nerve endings in the eye muscle spindles, though elaborate, are possibly simpler than the comparable endings in other somatic muscle. We feel that more work might profitably be done on a comparative study of nerve endings in the muscle spindles of the higher mammals and man, for we do not believe that detailed work on rabbits and cats can be applied directly to man. The pattern of nerve fibres at the poles of the eye muscle spindle is somewhat similar to the pattern of the motor supply of other somatic muscle spindles. There are many nerves associated with the capsules of the spindles. The eye muscle spindles are both shorter and thinner than other somatic muscle spindles and are more delicate structures. The description of the structure of eye muscle spindles given in this paper is perhaps reminiscent of the account of human fœtal muscle spindles (Forster, 1902; Cuajunco, 1940) and suggests that the human eye muscle spindle may be a rather primitive form of muscle spindle.

The number of muscle spindles in the human extrinsic eye muscles bears comparison with the number of muscle spindles seen in the lumbrical muscles of the human hand. These latter muscles have the highest muscle spindle count and are perhaps the most finely adjusted of all the somatic muscles. The distribution of the muscle spindles is not the same in the two sets of muscles. In the lumbricals the spindles are found scattered throughout the muscle but predominating in the belly, whilst in the eye muscles they are confined to certain specific regions of the muscle. In extrinsic eye muscles no muscle spindles have been found among the simple spiral endings or the motor endings in the belly of the muscle, but they are present in the proximal third and at the proximal end of the distal third of the muscles.

It is too soon to draw any conclusions about the fact that muscle spindles are present in the extrinsic eye muscles of some animals and not of others, but attention may be drawn to certain points. The voluntary movement of the eyes as we know it in man is probably far from widespread in animals, where neck movements largely take the place of extensive eye movements. A macaque money will leap about with great skill, but each motion is preceded by a quick turn of the head in the direction at which the animal is aiming, or if it sits watching something its eye movements are very small compared with the neck movements. It is in

the higher monkeys and man that eye movements are the most extensive, for sight is of the greatest importance, the foveæ are well developed, there is stereoscopic vision, and the co-operation between the eyes and the forelimbs has been enormously enhanced by the upright posture. We have found that the largest number of muscle spindles appear to be present in the human inferior rectus oculi muscle, and this finding may be associated with the constant pre-occupation of the eyes with the hands.

A large number of animals have no foveæ and do not depend, to any major extent, on eyesight. The senses of smell and hearing are, in these animals, of greater importance than that of vision and so the need for fine movements of the eyes is much less. The extrinsic eye muscles in these animals are not only devoid of muscle spindles but they are also far less richly supplied with nerve fibres. Such eye movements as occur are in response to the movements of the head and body and are postural.

Besides the higher monkeys, those animals that have been shown to have muscle spindles in their extrinsic eye muscles belong to some branches of the ungulates, many of them animals with a high centre of gravity calling for good balance. The remarkable balance of goats and deer may well be aided by impulses from the eye muscles. This group of animals seem to have some degree of convergence, for distinct eye movements, which are not postural, are seen. They have no fovea but there is a horizontal sensitive retinal band.

It is clear from the evidence presented in this paper that muscle spindles, the recognized sensory endings for the proprioceptive sense in somatic muscles, are present in all human extrinsic eye muscles and in the eye muscles of certain animals. Their function in these muscles must surely be similar to their function in other somatic muscles. They provide a tangible proof of sensory endings in the extrinsic eye muscles and they give to these muscles a means of recording their own activity. Little has been said here of the other nerve endings seen in human extrinsic eye muscles, but we would emphasize the remarkable wealth of the nerve supply, only a part of which is undoubtedly motor. The nerve endings found near or on the tendons, the spiral nerve endings, the elaborate nerve pattern seen at the periphery of the muscles and other complex nerve endings that we have not described, all suggest to us that there must be a large sensory element in the extrinsic eye muscles of man in addition to the proprioceptive supply undoubtedly provided by the muscle spindles.

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advice on photography. This study would have been impossible without the help of Mr. Ronald Beesley who has cut and stained large numbers of sections, and whose technical skill has aided us constantly.

Summary

Muscle spindles are present in all the extrinsic eye muscles in man. They are found only in certain regions of these muscles. The number of muscle spindles seen in human eye muscles is comparable with the number of muscle spindles found in the lumbrical muscles of the human hand. Forty-seven muscle spindles have been found in one human inferior rectus oculi muscle.

The muscle spindles in eye muscles differ from the muscle spindles in the more exposed skeletal muscles of the body in that they have very delicate capsules and in general are smaller.

Muscle spindles have also been found in the extrinsic eye muscles of the chimpanzee, but not in those of the macaque monkey or the other common laboratory animals (dog, cat, rabbit). They are present in the extrinsic eye muscles of members of certain branches of the ungulates.

Since muscle spindles form the main proprioceptive supply of other somatic muscles, it is assumed that the eye muscle spindles form a part of the proprioceptive supply of the extrinsic eye muscles in man.

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Since carrying out the work reported in this paper we have found a note on the occurrence of muscle spindles in human ocular muscles by E. Farquhar Buzzard (1908, *Proc. roy. Soc. Med.*, Neurological Section, **1**, 83 - 87). This paper gives an illustration of a transverse section of a spindle in an eye muscle from a case of myasthenia gravis, but gives no detail of its position in the muscle or of the frequency of such spindles, beyond saying that they are few or sometimes absent.

LEGENDS FOR PLATES

PLATE I

FIG. 2.—Transverse section through the proximal third of a human medial rectus oculi muscle. The polar region of a muscle spindle is seen. The capsule of this spindle is fairly complex (compare it with the capsule of the muscle spindle in fig. 7) and has a small blood-vessel incorporated in it (lower left) and also a small nerve trunk (lower right). There are seven intrafusal muscle fibres in this muscle spindle. These are separated by the connective tissue septa which are characteristically seen in the polar region. Capillaries are also seen within the capsule. There is no periaxial space.

Note the varying sizes of the extrafusal muscle fibres, including the very large one to the right of the muscle spindle. The many nuclei around this large muscle fibre belong mainly to the endothelial cells of adjacent capillaries and some to sheath of Schwann cells. A nerve trunk is seen to the right of the figure. (Paraffin section, hæmatoxylin and eosin.)

FIG. 3.—Transverse section through the distal third of a human rectus oculi muscle. A muscle spindle is seen, cut through the polar region. There appear to be two, concentric, capsules; an inner capsule, the true capsule of the muscle spindle, enclosing seven intrafusal muscle fibres and sending in fibrous septa amongst them, and an outer capsule, which is found only in the polar region and encloses a number of extrafusal muscle fibres. Two of the intrafusal muscle fibres have central nuclei. A capillary is seen within the true capsule, and several more within the outer capsule. A small nerve trunk is incorporated in the lower wall of the true capsule. (Paraffin section, hæmatoxylin and eosin.)

FIG. 4.—Transverse section through a rectus oculi muscle from an 82-year-old man. The muscle spindle seen has a thin capsule enclosing three intrafusal muscle fibres, a small nerve trunk (below the largest intrafusal muscle fibre) and several separate nerve fibres. There are some fine threads of connective tissue and a few capillaries within the capsule. Note the large diameter of one of the intrafusal muscle fibres. (Paraffin section, Holmes' "Silver on the slide" method, toned with gold chloride.)

FIG. 5.—Transverse section through the proximal third of a superior rectus oculi muscle from a boy aged 2. Two muscle spindles, cut through the equatorial region, are seen lying very close together. They are separated by two large extrafusal muscle fibres. A nerve trunk lies above and between the two spindles. The capsules of both muscle spindles are extremely delicate, and the periaxial space is prominent. Note the varying sizes of the extrafusal muscle fibres. (Paraffin section, hæmatoxylin and eosin.)

FIG. 6.—Transverse section through the distal third of a human lateral rectus oculi muscle. The muscle spindle seen has been cut through the region of the equator. The fibrous tissue capsule is thin and delicate and its nuclei are flattened. There are seven intrafusal muscle fibres, one having a central nucleus. There are fine connective tissue threads within the capsule and around the intrafusal muscle fibres, and a capillary is seen. The periaxial space is prominent. (Paraffin section, hæmatoxylin and eosin.)

FIG. 7.—Transverse section through the superior rectus oculi muscle of a 2-year-old child. The muscle spindle seen is cut through its equatorial region. There are four intrafusal muscle fibres, one with a central nucleus. Fine threads of connective tissue are seen around these intrafusal fibres, and a nerve fibre runs beside the muscle fibres. The capsule is delicate and has flattened nuclei. A small nerve trunk and blood-vessel are seen to the right above the spindle and the nuclei of a sheath of Schwann are seen to be incorporated in the capsule (above). (Paraffin section, hæmatoxylin and eosin.)

PLATE II

FIG. 8.—Longitudinal section through a human inferior rectus oculi muscle. A muscle spindle is seen crossing the field from top to bottom. The delicate capsule of this spindle is torpedo-shaped and encloses at least two intrafusal muscle fibres. These are of smaller diameter than the adjacent extrafusal muscle fibres and are separated from the capsule by the periaxial space. A small nerve trunk is seen at the upper right part of the field. This runs down to enter the spindle almost at its mid-point. A capillary runs along just inside the capsule on the left. (Paraffin section, Masson's trichrome stain.)

FIG. 9.—Longitudinal section through a rectus oculi muscle of a child. A muscle spindle crosses the field vertically, having a small nerve trunk running alongside it on the right. This is a very thick section and the mid-part of the spindle is seen in its entirety, though the ends both pass out of the section. The delicate capsule of the spindle is clearly visible in the upper part of the field. (Frozen section, stained by the Gros-Bielschowsky method.)

FIG. 10.—Very low power view of a longitudinal section through the central third of a human rectus oculi muscle. The dense band of nerve fibres, which is so characteristic a feature of this region, is seen crossing the field. The upper part of the figure shows the more proximal end of the muscle with the nerve trunks breaking into smaller bundles. The central part of the field, where the multitudes of nerve fibres form a dark band across the figure, is the zone of motor nerve endings. The lowest part of this dark band is the zone of simple spiral and other intricate nerve endings. The lowest part of the figure, the more distal part of the muscle, shows far fewer nerve fibres than are seen in the central band, though even here the muscle contains much greater numbers of nerve fibres than are ever seen in other somatic muscles. No muscle spindles have ever been seen in the region of the central dark band. (Frozen section, stained by the Gros-Bielschowsky method.)

FIG. 11.—Transverse section of a muscle spindle in a human medial rectus oculi muscle. A well-defined capsule is seen with a nerve trunk incorporated in its wall (on the left). Within the capsule there are three intrafusal muscle fibres, capillaries and an intricate arrangement of nerve fibres. One nerve fibre partly encircles the spindle, either just inside or within the walls of the capsule. (Paraffin section, Holmes' "Silver on the slide" method.)

PLATE III

FIG. 12.—Low power field of a transverse section through the distal third of a human inferior rectus oculi muscle. Four muscle spindles, A, B, C and D, are seen in this field. Spindle A has seven intrafusal muscle fibres and a nerve trunk is contiguous to the capsule (above and to the right). Spindle B has two intrafusal muscle fibres and a smaller nerve trunk is incorporated in its capsule (to the right). Spindle C has three intrafusal muscle fibres and its capsule is thicker than those of A and B. A nerve trunk is also incorporated in the wall of its capsule (on the left). Spindles A, B and C all show a fairly prominent periaxial space. Spindle D is cut through its polar region. Three intrafusal muscle fibres are seen in it, separated by the connective tissue septa which are characteristic of the polar region of a muscle spindle (compare with fig. 3). A small nerve trunk is seen in the wall of the capsule (below). (Paraffin section, Masson's trichrome stain.)

FIG. 13.—Comparable field with that seen in fig. 12. Several more sections had been cut from the block from which the section shown as fig. 12 was taken. Thus three of the spindles seen in fig. 12, spindles A, B and D, are seen again but

farther along their length. Spindle A still has seven intrafusal muscle fibres and its nerve trunk though smaller is in the same relative position. Spindle B still has two intrafusal muscle fibres, but its nerve trunk though adjacent is not now incorporated in the capsule. Spindle C has ended, though the intrafusal muscle fibres which have passed out of the end of the capsule to become extrafusal fibres can still be identified. The nerve trunk can also be seen. Spindle D still shows the characteristic architecture of the polar region, but has probably been cut nearer the equator, since an extra intrafusal muscle fibre is seen in the centre. Figs. 12 and 13 illustrate admirably the way in which serial transverse sections were used in order to determine the size and shape of muscle spindles. (Paraffin section, hæmatoxylin and eosin.)

FIG. 14.—Transverse section of a muscle spindle in a human rectus oculi muscle showing two intrafusal muscle fibres having large central nuclei. Note the thin capsule. A capillary is seen in the wall of the capsule (above). (Paraffin section, hæmatoxylin and eosin.)

FIG. 15.—Transverse section of the proximal end of a human rectus oculi muscle. A single encapsulated muscle fibre is seen, closely related to a nerve trunk. This is a muscle spindle with one intrafusal muscle fibre. (Paraffin section, Holmes' "Silver on the slide" method, toned with gold.)

FIG. 16.—Longitudinal section through a human inferior rectus oculi muscle showing a complicated nerve ending at the proximal musculo-tendinous junction. The lower part of the field shown is tendinous, the upper part is muscular. The large nerve fibre to the left of the field runs down towards the tendon of origin and then loops upwards to break up into complicated endings lying around and between the muscle fibres whose cross-striations can be seen. (Frozen section, stained by the Gros-Bielschowsky method.)

PLATE IV

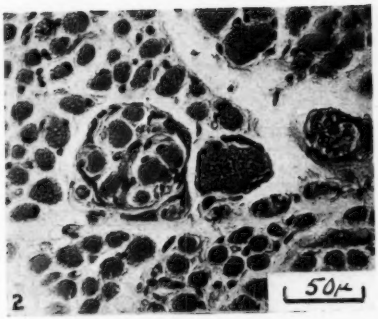
FIG. 17.—Transverse section through the middle third of a human rectus oculi muscle. This is the region that is very rich in nerve fibres. Many nerve fibres end by encircling single muscle fibres, to form simple spiral endings. These endings have no capsule. Several of them can be seen in this field. No muscle spindles are present in this area. (Paraffin section, Holmes' "Silver on the slide" method.)

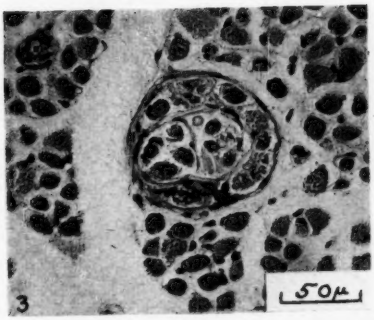
FIG. 18.—Transverse section through a human rectus oculi muscle from the same region as that shown in fig. 17. Two muscle fibres (one at the top and one at the bottom of the field) are encircled by nerve fibres. These are parts of simple spiral nerve endings. The sheaths of Schwann of these two encircling nerve fibres are clearly seen. A small nerve trunk and a number of individual nerve fibres are also seen. (Paraffin section, hæmatoxylin and eosin.)

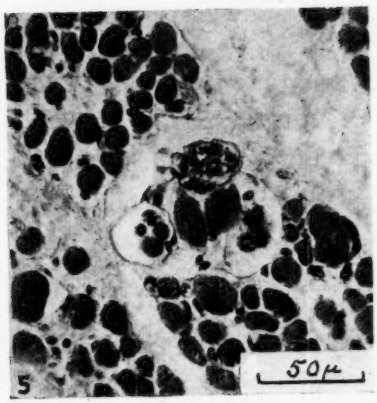
FIG. 19.—Transverse section through the proximal part of the middle third of a human rectus oculi muscle. Many small nerve trunks and branches are seen, giving this part of the muscle a very characteristic appearance. Compare the large diameter of some of the nerve fibres with the diameters of the muscle fibres. (Paraffin section, Holmes' "Silver on the slide" method, toned with gold chloride.)

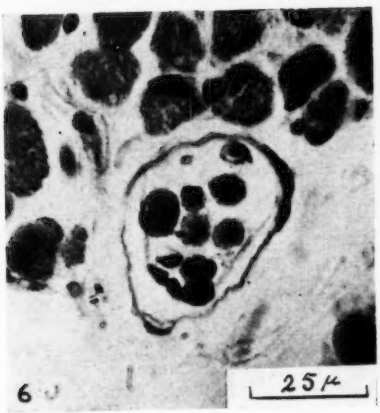
FIG. 20.—Transverse section through a first lumbrical muscle from a human hand. A double muscle spindle is seen. Compare the extremely thick capsule with the delicate capsules of the muscle spindles in eye muscles shown in Plate I. The closely packed extrafusal muscle fibres, polygonal in shape, should be compared with the more widely spaced, rounded muscle fibres characteristic of eye muscles, which are well seen in fig. 18. (Paraffin section, hæmatoxylin and van Gieson.)

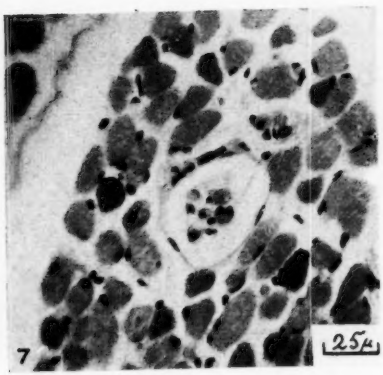
PLATE I





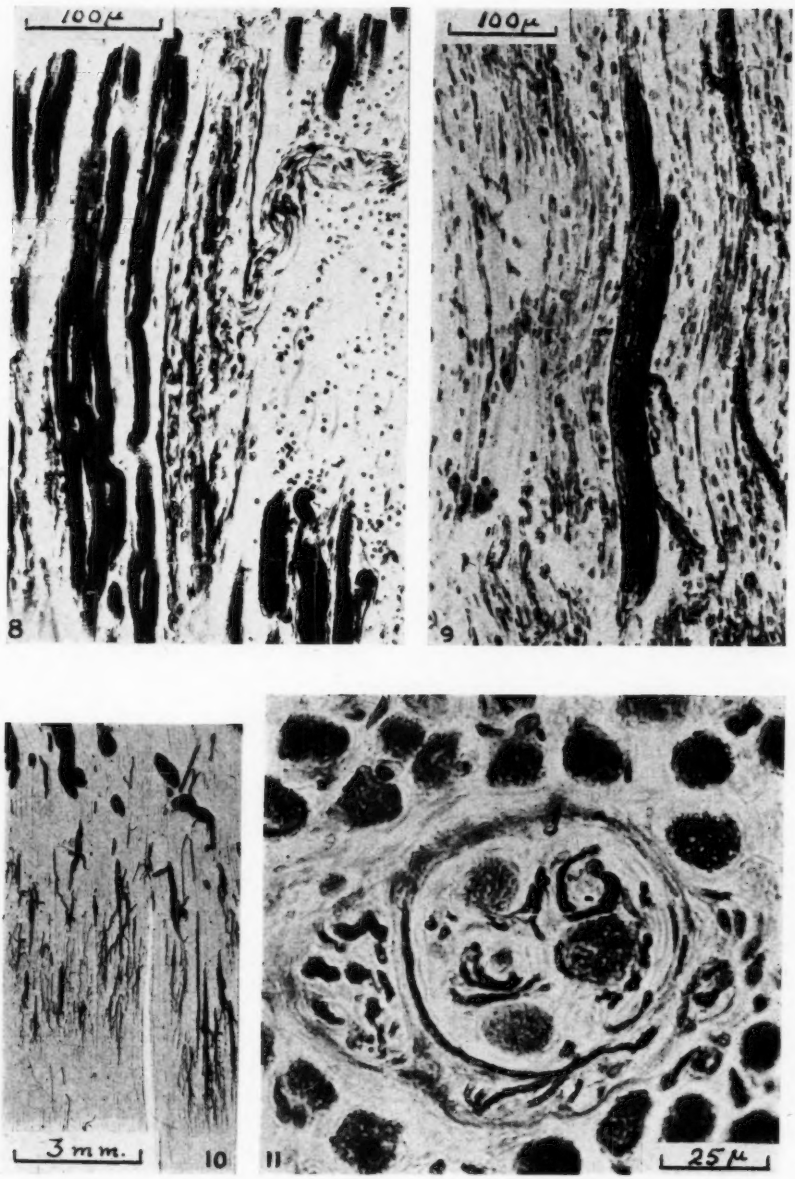






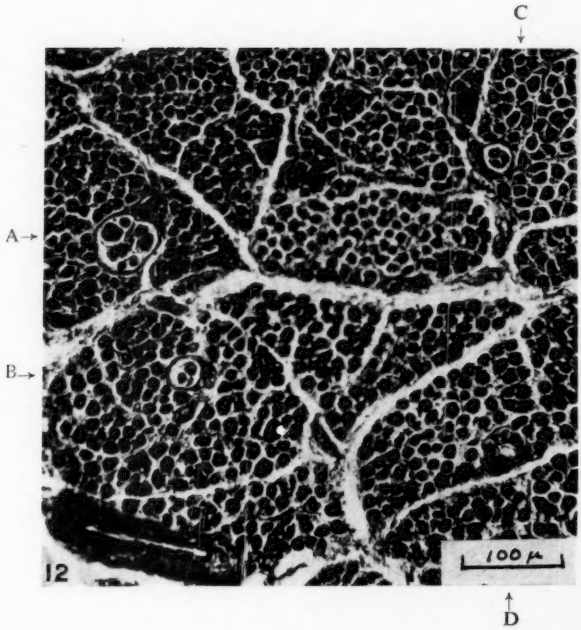
To illustrate article by Sybil Cooper and Peter M. Daniel.

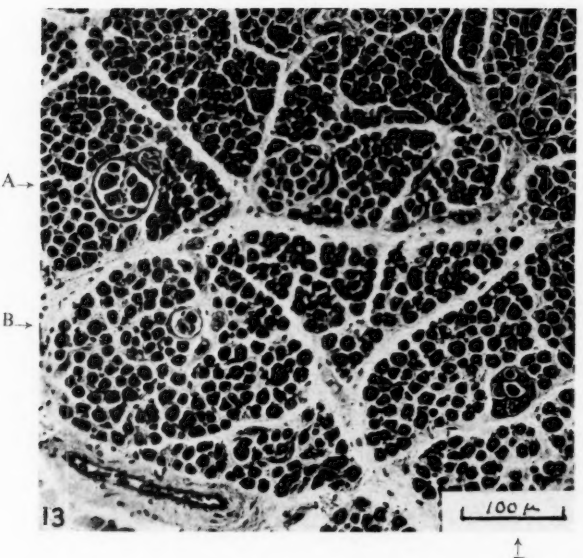
PLATE II



To illustrate article by Sybil Cooper and Peter M. Daniel.

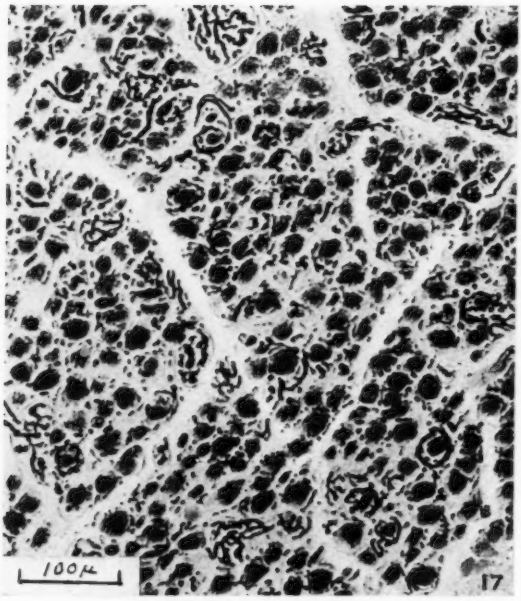
PLATE III

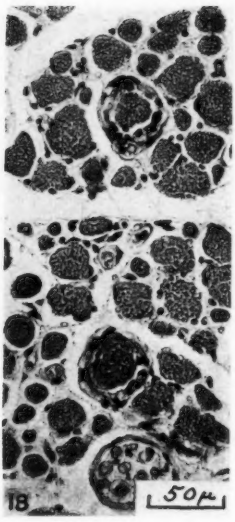


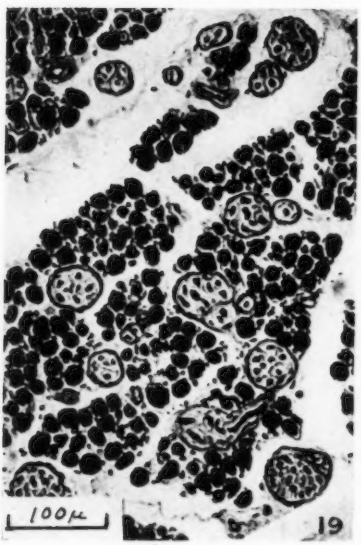


To illustrate article by Sybil Cooper and Peter M. Daniel.

PLATE IV







To illustrate article by Sybil Cooper and Peter M. Daniel.

ON AMYOTONIA CONGENITA

BY

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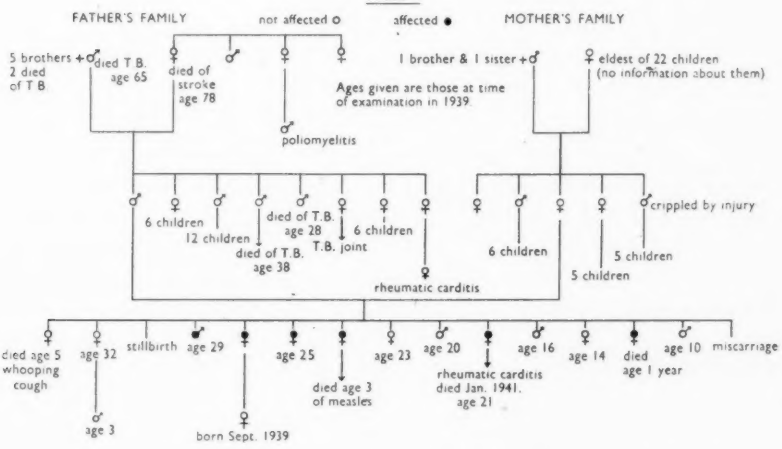
THE clinical picture of amyotonia congenita in infancy may change to that of a non-progressive myopathy in adolescence. A family which had been under observation for some years at the National Hospital in which this sequence of events was illustrated has previously been described (Aldren Turner, 1940); since then one affected member of the family who suffered from rheumatic heart disease in addition has died of endocarditis, and her brain and spinal cord have been examined pathologically. Full details of the family are available in the previous paper; briefly there were 13 children, of whom 6 were affected by the disease. An account of the collaterals of the family was not included in my previous paper—Table I

TABLE I



shows the details of this family history. Information on the family was obtained from the mother of the affected children, who was remarkably well informed about her own and her husband's relations, except that no details were available about her mother's 21 siblings. There were no other cases of neurological disease except for a first cousin once removed on the paternal side who had paralysed legs. This patient had been in the National Hospital under Dr. Tooth in 1911 when she was considered to be suffering from the effects of anterior poliomyelitis, the acute illness having

taken place a few weeks before admission. The only other possible neurological disorder was in a paternal grand-uncle who was said to have had a club-foot all his life, but no other details of this were available. The disease appeared in 6 siblings out of 13 while their 40 first cousins and 11 aunts and uncles were not affected by it.

The mother said that she could tell which children were going to be affected as fœtal movements were late in starting and were feeble with the affected children as compared with the normal ones. When they were born the affected children were abnormally limp and could be folded up into the shape of a ball. There was very little voluntary power in the legs until they were about 18 months old, and at the age of about 2 years they started to propel themselves along the floor on their buttocks. There was no delay in speaking and mental development was normal.

Five of the children were examined at the National Hospital, when under the care of Dr. F. E. Batten, in early childhood and showed the typical physical signs of amyotonia congenita. There was extreme flaccidity so that the limbs could be placed into abnormal positions, the muscles felt flabby, but no localized muscle wasting was noted, and the tendon-jerks were absent except in two examined for the first time when aged 3 and 4, in whom the ankle-jerks were present. Two of the affected children died in childhood, one aged 3½ of measles and one aged 12 months of an unknown cause. The other 4 developed in a similar manner, the hypotonia gradually became less and as this occurred localized muscular wasting appeared.

The whole family was examined in 1938 and no abnormality was found in any of the 6 children who had been normal at birth, except that two of them showed slight weakness of the triceps relatively to the other muscles and moderate diminution of the triceps-jerk. The parents showed no signs of muscular disorder. The four affected members who were examined in 1938, when under the care of Dr. Critchley, were then aged 29, 27, 25, and 18, and the clinical picture was essentially the same in all. There was no hypotonia but there was marked localized muscular atrophy, the same muscles being involved in each case. The most wasted muscles were the sternomastoids, the pectorals, the trapezii and the triceps, while there was also considerable atrophy of the serratus magnus, the spinati, the latissimus dorsi, and in three cases of the deltoids. The wasted muscles were weak in proportion to the wasting. There was no apparent localized wasting of the leg muscles except of the quadriceps femoris, but in all 4 there was slight weakness of flexion and extension of the hips and extension of the knees. 3 of the patients walked in a waddling manner with a lumbar lordosis, while the fourth walked normally.

In all 4 the triceps and knee jerks were absent, while the other tendon-

jerks were normal. The abdominal reflexes were present and the plantar responses were flexor. There was no fasciculation, no myotonia on voluntary movement or percussion, and no sensory impairment. The condition did not appear to be progressive and 3 of the patients were able to earn their livings in moderately strenuous occupations, while the fourth was incapacitated by rheumatic heart disease. The patient with rheumatic heart disease died of endocarditis in 1941.

Case history.—F. S., a girl, was the tenth child. Birth-weight 6 lb. Forceps delivery. She was born with weakness and hypotonia of all muscles, the arms being less affected than the legs. After the age of 1 year there was gradual slow improvement.

She was admitted to the National Hospital under Dr. Risien Russell in 1924 when she was 4 years old. There was marked hypotonia of the limbs and trunk. The muscles were not wasted and were of fair power except that there was winging of the scapulæ. The biceps and triceps jerks were absent and the other jerks present. She had difficulty in sitting up.

After this she improved slowly and was admitted again under Dr. Critchley in 1931 when she was aged 11. She still had some difficulty in running and she seemed to trip over things more than normal.

On examination there was no longer any hypotonia. Facial movements were normal. There was marked wasting of the sternomastoids, and slight wasting of the trapezii, deltoids, spinati, and thenar muscles. There was winging of the scapulæ. Power was proportional to the wasting. Some weaknesses of the erector spinæ on both sides. The legs were thin but there was no localized wasting or weakness. The triceps-jerks were absent, the biceps, supinator, and knee jerks were just obtained, and the ankle-jerks were normal. She walked with a slow waddle and lumbar lordosis. There was also slight enlargement of the heart, aortic systolic and diastolic murmurs were present.

During the next seven years she had two attacks of rheumatic fever, which necessitated her spending a good deal of time in bed, and in April 1938 she was readmitted under Dr. Critchley suffering from rheumatic fever.

On examination there was considerable dyspnœa and evidence of mitral stenosis and aortic regurgitation. When the cardiac condition had settled down sufficiently for examination of the nervous system she was found to have practically absent sternomastoids, pectorals, and latissimi and triceps; marked wasting of the spinati, trapezii, serrati, and deltoids; and slight wasting of the biceps, rhomboids, and forearm muscles. There was flattening of the thenar eminences and a contracture of the little finger of the right hand. There was no localized wasting of the legs except for quadriceps femoris but there was some weakness of flexion and extension of the hips and knees. The triceps and knee jerks were absent and the other jerks present, the ankle-jerks being considerably brisker than the others. Plantar responses were flexor. After four months in hospital she was able to walk fairly well with a slight lumbar lordosis. Electrical reactions of the muscles were normal.

A biopsy of the left triceps was made. The section showed chiefly fatty and fibrous tissue. In the latter there were a very few thin muscle fibres and one large muscle fibre, cut obliquely, was also seen. The nerves appeared to be well myelinated but the only muscle spindle seen was rather degenerated. The small muscle fibres remaining showed a trace of cross striation. From the extreme scantiness of fibres it was impossible to say whether the condition was myopathic or not.

She was readmitted under Dr. Critchley in February 1939 on account of increasing dyspnœa and in April 1939 a complete thyroidectomy was performed by Mr. Julian

Taylor in an effort to alleviate the congestive heart failure. There was some improvement following this but in July 1940 she began to have attacks of abdominal pain, retching, and vomiting, and she ran a low-grade fever. She was readmitted in August 1940 under Dr. Granger Stewart and died of endocarditis in January 1941. There was no essential change in the neurological and muscular condition during the last two years of her life.

Pathological examination was carried out by Dr. Greenfield, and the following is his report on the findings:

Post-mortem forty-eight hours after death.

The body of a very slight young woman.

Heart: Old-standing mitral valvular disease with large partly calcified verrucose masses on the cusps of the valve. No macroscopical or microscopical evidence of persistence of rheumatic disease.

Fairly large recently infarcted area in the *spleen*.

The *lungs* showed œdema and bronchopneumonia.

The *liver* showed a slight degree of cirrhosis with a general excess of collagenous fibres but no thick fibrous septa. The liver cells are shrunken and many contain fatty globules and there is general dilatation of the intertrabecular sinusoids. The condition is one of chronic nutmeg liver with little evidence of recent excess of back pressure.

Sections were taken from the following segments of the *spinal cord*: 1st and 8th cervical, 1st and 6th thoracic, 2nd, 3rd and 4th lumbar and 2nd to 3rd sacral.

Sections stained by the Weigert-Pal method showed no tract degeneration. In sections stained by toluidin blue for Nissl granules there was no evidence of loss of anterior horn cells. These appeared normal except for a very occasional cell in the lumbar and sacral segments in which there were slight chromatolytic changes such as eccentricity of the nucleus and powderiness of the more centrally placed Nissl granules. By comparison with the cord of a normal adult sectioned at the same thickness and stained in the same way, there was no significant difference either in the size or the number of motor neurones, although in both cases the counts in the various groups in the different segments were rather lower than those given in Bruce's Atlas. This will be clear from the accompanying table.

TABLE II.—COUNTS OF ANTERIOR HORN NEURONS AT DIFFERENT LEVELS IN (1) PATIENT, (2) NORMAL ADULT, AND (3) AS GIVEN IN BRUCE'S ATLAS

		(1)	(2)	(3)
Level	*Group*	*Patient (F.S.)*	*Normal Adult*	*Bruce's Atlas*
C.8	Antero-median	8 small	6 small	7 small
	Lateral	29 large	26 large	31 large
Th.1	Antero-median	5 small	15 small	7 small
	Lateral	26 larger	16 larger	28 larger
L.2.	Antero-median	10 medium	10 medium	11 medium
	Lateral	25 medium to large	10 large	36 large
L.3	Antero-median	4 medium	6 medium	5
	Lateral	24 larger	30 large	35
L.4	Antero-median	10	10	10 small
	Lateral	33	44	74
S.3	Antero-median	10		5
	Lateral	22		29

Sections were also made from representative parts of the brain including the motor cortex, the hippocampal formations, the basal ganglia and cerebellum. These

showed no abnormality; in particular the Betz cells of the motor cortex were normal in number and size. Several lumbar dorsal root ganglia were also examined without the discovery of any definite abnormality.

The following muscles were examined microscopically: the gastrocnemius, tibialis anticus, biceps femoris, quadriceps extensor femoris, ilio-psoas, deltoid, and flexor profundus digitorum.

In all, the muscle fibres were rather small, most of them measuring from 20 to 30 μ. A few were as much as 50 μ in their narrower diameter. Sarcolemmal nuclei appeared rather more numerous than normal, as is usual in atrophied muscle. The degree of atrophy in most of the muscles was, however, no greater than would be expected in a patient who had been bedridden for some months.

In the more affected muscles, especially the quadriceps femoris groups, more specific alterations were seen. These consisted in central nuclei, often arranged in chains, in otherwise normal muscle fibres and isolated fibres which had undergone hyaline change, no longer showing transverse striation in longitudinal section or division into sarcostyles in transverse sections. They were being invaded from the surface by histiocytic cells which were scanty in some but very numerous in others. The number of fibres undergoing this type of degeneration was small as would be expected in so chronic a condition, but in the fibres seen was of the same character as the degeneration seen in myopathic muscle. These muscles also contained small groups of sarcolemmal nuclei probably indicating the disappearance of muscle fibres, and in places the loose arrangement of fibres and the large amount of interstitial fat in a bundle conveyed the same impression.

Summary of Pathological Findings

No significant changes were found in the anterior horn cells or in the tracts of the spinal cord, and there were no changes in the areas of the brain which were examined. Counts of the number of anterior horn cells at different levels of the spinal cord showed no appreciable difference in similar counts in a normal adult. The fact that in both the patient's spinal cord and in that of a normal adult there were rather fewer anterior horn cells than the figures given in Bruce's Atlas is not thought to be significant.

Atrophic changes were found in the muscles, in many of them atrophy was compatible with the fact that the patient had been bedridden for several months, but in the more severely wasted muscles more specific changes were found. There was degeneration of the muscle fibres and invasion by histiocytic cells. These changes were of a similar type to those found in the myopathies.

The Myopathic Type of Amyotonia Congenita

In my previous paper I suggested on clinical grounds that the affected members of the family were suffering from a congenital myopathy, which had in early life presented the typical picture of amyotonia congenita, and the pathological findings now available confirm this suggestion. When amyotonia congenita was originally described by Oppenheim (1900) under the name of myatonia congenita he suggested that the condition was due

to a delayed and disordered development of the musculature and that there was no disease of the central nervous system. In the earlier years of the century there was considerable argument as to whether the condition should be considered as a myopathy or not. Collier and Wilson (1908) and Collier and Holmes (1909) argued on a number of grounds that amyotonia congenita was quite distinct from the myopathies but stated that the relationship between the conditions could only be determined with certainty when a much larger number of clinical and pathological records were available. Batten (1909–1910 and 1910) thought that it was impossible to make any dogmatic statement as to the relationship of what he called the simple atrophic type of muscular dystrophy to amyotonia congenita, but thought that some of the cases of the latter condition almost certainly belonged to the myopathic group.

As post-mortem records on patients with amyotonia congenita began to accumulate it was apparent that in the majority of cases there were pathological changes in the spinal cord, particularly in the anterior horn cells, which excluded the cases from the group of myopathies. There were, however, exceptions to these findings of spinal changes. The first case in which no abnormality was discovered in the spinal cord was that of Spiller (1905); Greenfield and Stern (1927) thought that this was an anomalous case as there appeared to have been mental retardation and general malnutrition which might account for the hypotonia, which was not noted till the age of 5 months. Lerebouillet and Baudouin's (1909) case in which no pathological changes in the spinal cord were found has also been criticized on clinical grounds as shortly before death from bronchopneumonia the child had several fits, and the muscle hypotonia was replaced by spasticity.

Councilman and Dunn (1911) described a patient in which there was no doubt about the diagnosis of amyotonia congenita, and careful pathological examination showed no abnormality in the central nervous system. Similar cases with no abnormality in the spinal cord have subsequently been published by Haushalter (1920), Silberberg (1923), and Menges (1931).

Clinically a case resembling those in the present family and demonstrating a very close relationship between some cases of amyotonia congenita and myopathy was described by Silvestri (1909). Two children from the time of birth had marked hypotonia of the trunk and limbs with abnormal range of passive movements at the joints, while a maternal aunt suffered from the Landouzy-Dejerine type of myopathy. The elder of the two children gradually improved as he got older and when he was examined at the age of 6 the clinical condition was that of a muscular dystrophy of the Erb type. This case shows clearly the transition from the picture of amyotonia congenita in infancy to that of a myopathy in

adolescence, a transition shown also by the 4 affected members of the family described in this paper.

There seems to be no doubt from the clinical and pathological findings in my case that the clinical picture of amyotonia congenita can be caused by primarily muscular disorder of myopathic type without disease of the central nervous system, and the other cases recorded from the literature are in agreement with this view. Batten's suggestion of 1910 as to the myopathic nature of some cases of amyotonia congenita is fully confirmed.

Amyotonia of Spinal Cord Origin

Pathological reports in the literature show that only a minority of the cases of amyotonia congenita are of myopathic origin: in the larger number changes in the spinal cord have been found. Greenfield and Stern (1927) reviewed the previous cases in which post-mortems had been done and described the findings of four personal cases, in which the diagnosis of amyotonia congenita had been made in three and of Werdnig-Hoffmann's disease in the fourth. They made the important observation that there was no difference in the pathological findings in the spinal cord or in the muscles in the two conditions, and they considered them to be essentially the same disease process though clinical symptoms generally appeared some months after birth in Werdnig-Hoffmann's disease, and were present from the time of birth in amyotonia congenita. In their cases they found evidence of degeneration of anterior horn cells afforded both by definite chromatolytic changes in some of the cells and by the presence in sections stained by the Weigert-Pal method of "empty beds." These "empty beds" in some cases contained small shrunken cells which did not fill them, while others contained neuroglial tissue. These findings undoubtedly mean that normal anterior horn cells had been present at one time and had later degenerated.

Grinker (1927) who reported the pathological findings of one case of amyotonia congenita found a paucity of anterior horn cells and the presence of small cells, poor in chromatin without glial or vascular changes. He suggested that there was no definite clinical differentiation between amyotonia congenita and Werdnig-Hoffmann's disease, the two merging into one another. Pathologically there were two different types of spinal cord change: in one which he called the Werdnig-Hoffmann type there was degeneration of anterior horn cells with chromatolysis and neuronophagia; in the other, the Oppenheim type, there was a paucity of anterior horn cells and the presence of abnormal cell types without evidence of degeneration. He thought that the fundamental difference between the two types was only a question of the time at which the ganglion cells were affected.

More recent pathological reports have shown similar differences in findings in the central nervous system. Conel (1938 and 1940) has made a thorough study of two typical cases of amyotonia congenita at the ages of 4 months and 5½ months respectively. He found three degrees of severity of cell change in the anterior horns: an early stage with the nucleus and Nissl bodies crowded against the cell wall; an intermediate stage with clumps of granules in the cytoplasm; and a late stage with shrinkage of the affected cells. In addition he confirmed Greenfield and Stern's observations of "empty" spaces left as a result of cell atrophy. These cellular changes were found in the giant pyramidal cells of Betz and in some of the motor nuclei of the cranial nerves as well as in the anterior horn cells of the spinal cord. In all the areas affected there were normal cells as well as abnormal ones, and he felt certain that gradual degeneration of the cells had taken place. Macleod and Macdonald (1942) in two cases also found evidence of degenerative cell changes in the anterior horns: there was a great reduction of cells and the ones remaining were much reduced in size, shrunken, and altered in shape, and many of the nuclei were pyknotic. A few of the cells showed satellitosis being surrounded by a group of small glial cells which they thought indicated a progressive degenerative process. Hassin (1942) in one case also found evidence of a glial reaction and marked heterotopia of the anterior horn cells, especially in the lumbosacral segments.

All these findings support Greenfield and Stern's conclusions, that a degenerative process in the anterior horn cells is the basic pathology in the spinal type of amyotonia congenita. A different point of view is held by Freeman *et al.* (1945 and Freeman, 1946). Post-mortem examination of 5 clinically typical cases was made and similar changes were found in all. There was absence of the large multipolar Betz cells in the motor cortex, a paucity of anterior horn cells, and decreased myelination of the anterior roots without any evidence of degenerative changes in the spinal grey matter. They consider amyotonia congenita to be the result of a developmental defect which involves both the giant pyramidal cells of the motor cortex and the anterior horn cells of the spinal cord with resulting hypoplasia of the muscles; in fact a defective development of the whole motor system from the precentral gyrus to the muscles.

Conclusions

Amyotonia congenita is a clinical syndrome which can result either from a primarily muscle disorder, an infantile myopathy which may not be progressive, or from an affection of the spinal cord. Batten originally put forward the view that some cases were myopathic, Spiller (1914) pointed out that the symptom complex of amyotonia might result either

from a purely muscular condition or might be associated with changes in the anterior horn cells, and Brandt (1946) has recently re-stated this view. The clinical and pathological findings in the family reported here confirm the primarily myopathic nature of some cases of the disorder.

It is difficult to reconcile the spinal cord findings of different observers, and it is possible that there may be two distinct pathological processes which can cause the same clinical picture, a developmental defect of the anterior horn cells and the giant pyramidal cells, as described by Freeman, or a degenerative process affecting primarily the anterior horn cells. If this degenerative process occurs early enough the clinical picture of amyotonia congenita results: if it starts some weeks or months after birth the condition is that usually described as Werdnig-Hoffmann disease.

Summary

The clinical picture of amyotonia congenita in infancy can change into that of a non-progressive myopathy in adolescence. A family illustrating this transition is described.

Pathological examination in one member of the family showed no abnormality in the central nervous system and atrophy of the muscles of myopathic type.

Amyotonia congenita may result either from an affection of the spinal cord or from a primarily muscular disorder, a non-progressive myopathy.

Acknowledgments

I wish to thank Dr. Greenfield, who performed the pathological examination of the patient and supplied the photomicrographs, Dr. Macdonald Critchley who has been interested in the family described for many years, and the Medical Committee of the National Hospital, Queen Square, for permission to use the hospital records in the preparation of this paper.

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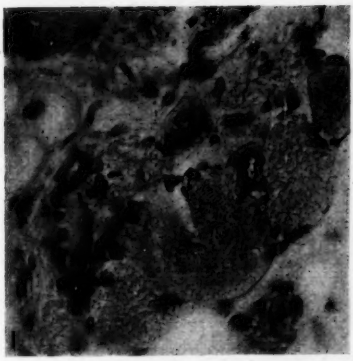
LEGENDS FOR PLATE

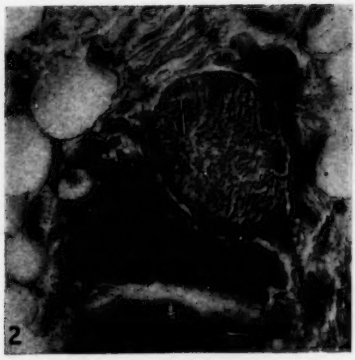
FIGS. 1 and 2.—Transverse section of biceps femoris ×400 showing histiocytic invasion of a degenerated muscle fibre. Note the absence of obvious sarcostyles in degenerated fibre in fig. 1.

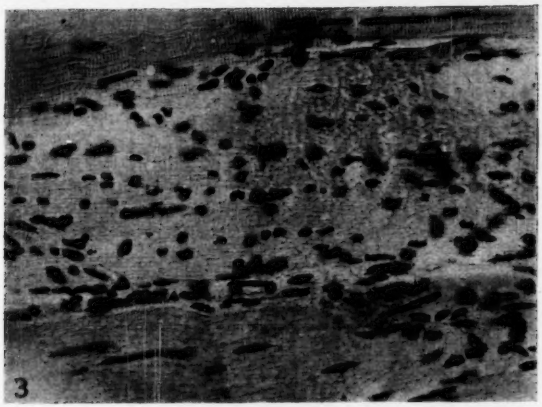
FIG. 3.—Longitudinal section of left quadriceps femoris ×400 to show histiocytic infiltration of a degenerated muscle fibre which has lost its transverse striation.

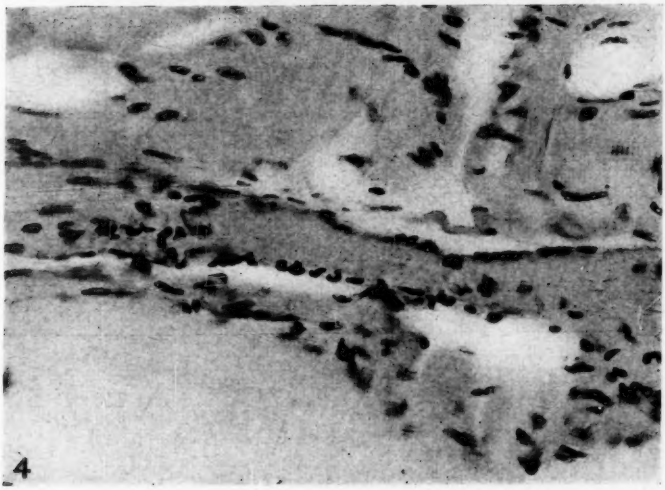
FIG. 4.—Longitudinal section of left quadriceps femoris ×500 to show early, chiefly superficial, histiocytic infiltration of a degenerated muscle fibre.

PLATE V









To illustrate article by J. W. Aldren Turner.

PROPRIOCEPTION AND THE MOTOR CORTEX

BY
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Laboratory of Neurophysiology, Department of Physiology, University of Minnesota.

It was shown in a preceding paper (Gellhorn, 1948) that alterations in posture influence quantitatively the movements resulting from stimulation of the motor cortex in the monkey. The postural changes consisted in varying the angle of a joint just prior to the application of the cortical stimulus. If, for example, the elbow formed an obtuse angle the reactivity of the biceps was greater than when the elbow was placed at an acute angle; conversely the latter condition was shown to enhance the reactivity of the triceps. The experiments seemed to show the validity of the von Uexkull-Magnus rule according to which central excitation has a tendency to flow into the stretched muscle. Our observations indicated, however, a definite limitation of this rule. Whereas Magnus observed that even the type of reflex movement depended on proprioceptive impulses which occurred in a certain posture no qualitative but only quantitative changes of cortically induced movement were seen in our earlier studies in different postures.

The present investigation is a further attempt to determine the effect of proprioception on movements induced by stimulation of the motor cortex and to reconsider the organization of the motor cortex in the light of these experiments.

In order to make these afferent impulses more effective than they were in the experimental conditions reported in the preceding paper one or more joints of an extremity were flexed or extended and fixated in this position while the cortex was stimulated. This procedure resulted regularly in very marked changes in the responses of the muscles to electrical stimulation of the motor area as disclosed by electromyographic records.

METHOD

The experimental technique is essentially the same as described in earlier studies from this laboratory (Murphy and Gellhorn, 1945; Bosma and Gellhorn, 1947; Gellhorn, 1948). Condenser discharges were applied through bipolar electrodes to the motor cortex of the monkey (*Macacus rhesus*) and the resulting electromyograms were recorded with an ink-writing oscillograph (Offner). An accurate map of the cortical area was made and the various foci were stimulated with electrodes orientated by the Horsely-Clarke apparatus. The period of stimulation was five seconds and the intensity at or slightly above threshold. The joint was fixated either manually or by adjustable metal braces which permitted the fixation of one or more joints of the arm or leg.

RESULTS

1. *The effect of fixation of a joint on the cortically induced electromyogram of the hind-leg.*—Whereas in the preceding paper and in the

[1] Aided by a grant from the National Foundation for Infantile Paralysis.

study of Loofbourrow the effect of cortical stimulation was studied on muscles with varying initial length the present experiments are concerned with the responsiveness of muscles which are allowed to shorten as compared with that of fixated muscles. An experiment in which the knee was respectively fixed and free at 110 degrees is reproduced in fig. 1 and

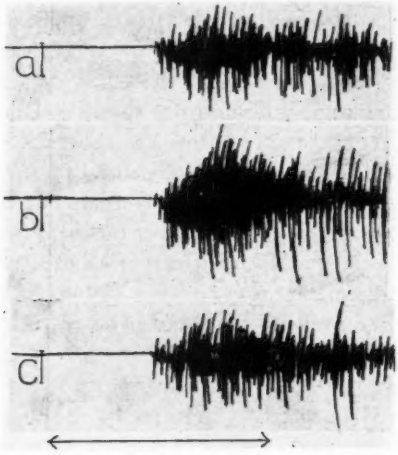

FIG. 1.—Stimulation of site[1] 13 with 1·9 volts for five seconds (arrow). Calibration: 150 microvolts. EMG of hamstrings (semitendinosus and semimembranosus); a and c knee at 110 degrees not fixated, b at 110 degrees but fixated.

shows that under fixation the amplitude of the EMG of the hamstrings is markedly increased. Fig. 2 shows an experiment in which knee and ankle were fixed at an angle of 160 degrees and compared with the reactivity of the muscles at a less obtuse angle without fixation. Here again a great increase is seen in the flexor muscles (in this case in the hamstrings and in the anterior tibial) under conditions of fixation.[2] The gradual increase in amplitude suggests that as a result of proprioception more motor units are called into action. These effects are marked and regular (cf. also fig. 12). Even those cases in which alteration of the angle of a joint failed to alter the EMG when the joints were free showed the increase in EMG response distinctly when the joint was fixed.

For this reason the following experiments are concerned only with the effect of fixation of one or more joints at an acute and obtuse angle in

[1]The stimulated cortical foci are given the numbers shown in the diagram of fig. 1 of the paper by Bosma and Gellhorn (1947).

[2]The slight increase in the EMG of the gastrocnemius seems to be due to co-innervation (cf. Bosma and Gellhorn, 1945).

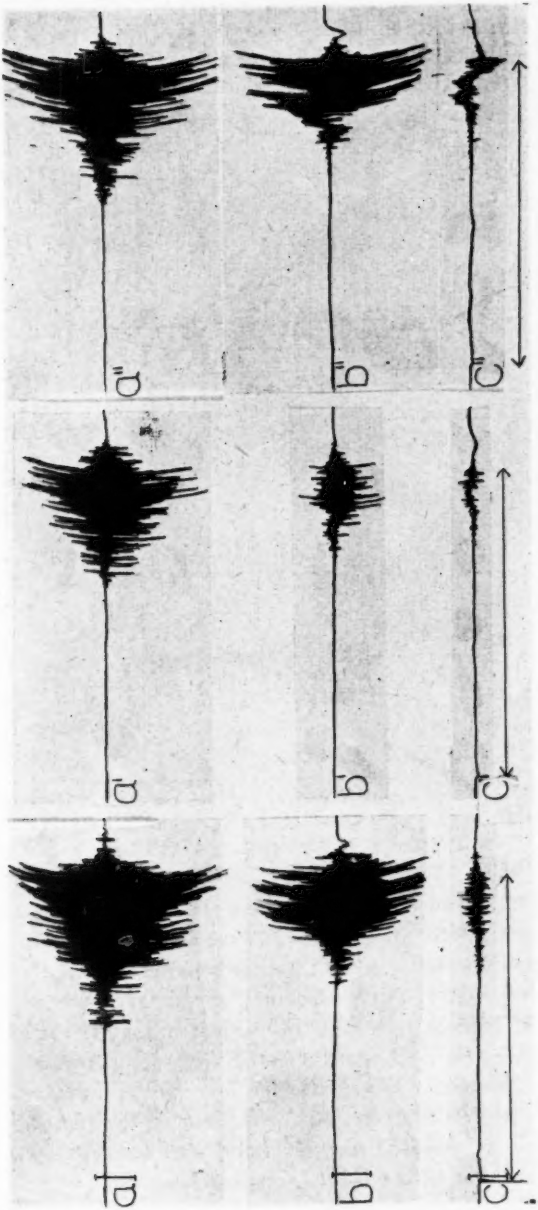

FIG. 2.—Stimulation of site 13 - 33 with 1·9 volts for seven seconds. Calibration: 150 microvolts; a to a″ hamstrings, b to b″ tibialis; c to c″ gastrocnemius. Left (a to c) and right figure (a″ to c″) knee and ankle fixated at 160 degrees; middle figure (a′ to c′) knee 90 degrees, and ankle 110 degrees not fixated.

order to maximize proprioceptive impulses. The first group deals with cortically elicited EMGs of the hind-leg.

Fig. 3 shows the effect of cortical stimulation of a medial (hind-leg)

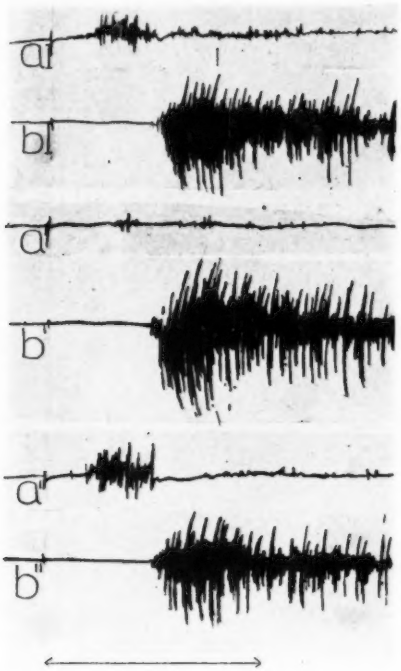

FIG. 3.—Stimulation of site 4 with 2·9 volts for five seconds. Calibration for a to a″ 50 microvolts, for b to b″ 150 microvolts; a to a″ quadriceps, b to b″ hamstrings; a, b and a″, b″ knee fixated at 45 degrees, a′ b′ knee fixated at 110 degrees.

site on quadriceps and hamstring muscles. In the actual experiment the EMGs of gastrocnemius and anterior tibial were also recorded. The reaction begins with the quadriceps in both positions (knee fixed at 45 degrees and 110 degrees respectively). On cessation of this response the hamstrings contract and their activity is accompanied by that of the anterior tibial muscle[1]. Fig. 3 illustrates that the activity of the quadriceps is considerable with the knee fixed at 45 degrees but it is only minimal when the knee is at an angle of 110 degrees. The behaviour of the hamstrings is, as was expected, just the opposite and the changes are reversible. In spite of the marked alterations in the E.M.G. response induced by changes in

[1] No activity appears in the gastrocnemius. Since different positions of the knee failed to change the activity of the foot-movers their record is omitted.

posture it should be emphasized that the pattern of response remains unchanged. The cortical focus used in this experiment is apparently one which induces a phasic response in the hind-leg similar to that described in an earlier paper for the fore-limb (Bosma and Gellhorn, 1947). The initial phase consists of a contraction of the quadriceps followed by activity in hamstrings and anterior tibial. The peripheral (proprioceptive) conditions which change quantitatively the response in quadriceps and hamstrings do not alter their sequence. Moreover, the hamstring response, even when reduced by fixation of the knee at 45 degrees, is much greater than that of the quadriceps under optimal conditions when this particular cortical site is used.[1]

Another example showing the influence of proprioception induced by fixation of these muscles is reproduced in fig. 4. Here again the quadriceps

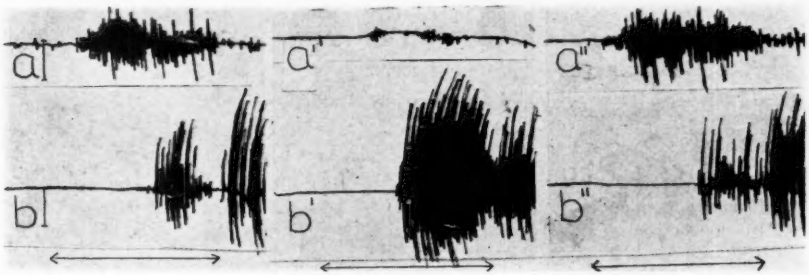

FIG. 4.—Stimulation of site 4 - 5 with 2·3 volts for five seconds. Calibration: 50 microvolts; a to a″ quadriceps, b to b″ hamstrings. Knee fixated at 45 degrees in a, b and a″, b″; knee fixated at 165 degrees in a′ b′.

precedes the hamstrings in activity. The different conditions of fixation alter profoundly the EMG of these muscles without, however, producing any change in the pattern of movement. The EMGs obtained at 165 degrees show that the great activity of the hamstrings does not start until the now minimal activity of the quadriceps has apparently ceased. Within these limits the summation time of the hamstrings varies inversely with the intensity of the muscular response as the figure indicates. It is also worthy of note that the hamstrings show a distinct after-discharge in maximal and minimal position in fig. 4 whereas the quadriceps even in the maximal position fails to show more than a trace of an after-discharge. The second period in the activity of the quadriceps (fig. 4, a′) appears to be due to a slight co-innervation due to the high degree of activity of the agonist (hamstrings).

[1] The activity in the quadriceps accompanying the maximum of hamstring activity is due to co-innervation.

In the experiment of fig. 5 the action of simultaneous fixation of knee and ankle at different angles is illustrated. When these joints are fixated

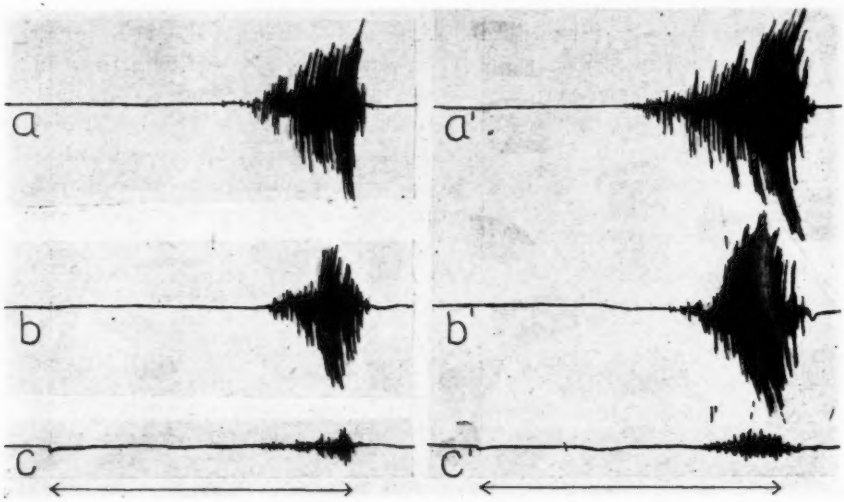

FIG. 5.—Stimulation of site 13 - 33 with 1·9 volts for seven seconds; a, a′ hamstrings, b, b′ tibialis, c, c′ gastrocnemius. Knee and ankle fixated respectively at 40 degrees and 75 degrees in left figure; fixation of both joints at 160 degrees in right figure.

at an acute angle the knee and ankle flexors show a lesser amplitude in their EMG than at an obtuse angle. The activity of the gastrocnemius (co-innervation) increases with that of the tibialis muscle. Finally, fig. 6

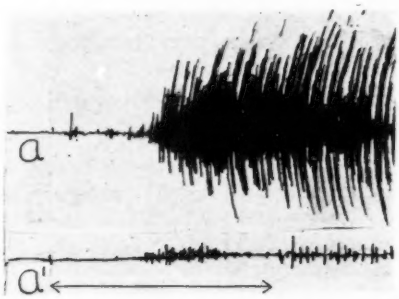

FIG. 6.—Stimulation of site 3 - 13 with 2·9 volts for five seconds. EMG of tibialis: a, ankle fixated at 180 degrees, a′ fixated at 35 degrees.

shows an enormous difference in the response of the tibialis when the ankle is fixed at two extreme angles. It is interesting to note that fixation

of the ankle at an obtuse angle (plantar flexion) not only increases the response of the tibialis during stimulation but induces a strong after-discharge as well.

II. The effect of fixation of a joint on the cortically induced electromyogram of the fore-leg.—Fig. 7[1] shows the influence of fixation on the

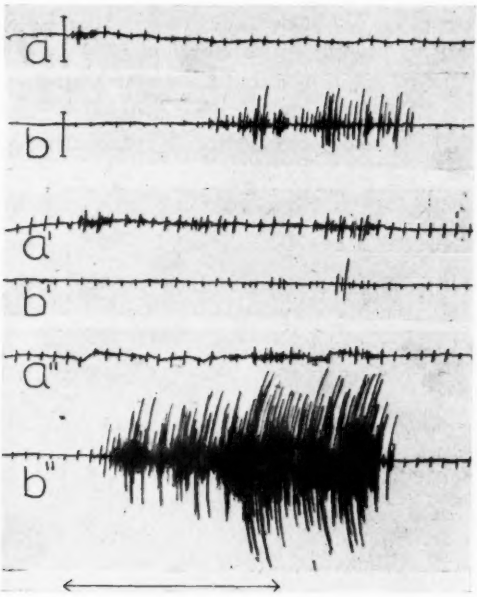

FIG. 7.—Stimulation of site 8 with 2·3 volts for five seconds. Calibration: 50 microvolts; a to a″ triceps, b to b″ biceps. Elbow at 140 degrees not fixated in a, b; elbow fixated at 45 degrees in a′ b′; elbow fixated at 140 degrees in a″, b″.

EMG response induced by stimulation of a cortical focus located in the reversal area of the fore-leg. Under control conditions when the elbow is not fixed, a small EMG appears in the triceps immediately on stimulation; this is followed, after a long delay, by a somewhat more conspicuous response of the biceps. With the elbow fixed at 45 degrees the triceps response is still very slight, although somewhat larger than under the previous conditions. The main effect, however, appears in the biceps, which is completely inhibited. On the other hand, if the elbow is fixed at 140 degrees the initial triceps response is suppressed and the biceps reaction is greatly increased. Changes in after-discharge parallel the degree of response recorded during stimulation. It is worthy of note that

[1] The small regular potentials seen in this and several other figures showing EMGs of upper arm muscles are due to the EKG.

in spite of the enormous changes in the response of biceps and triceps as a result of proprioceptive stimulation, the basic pattern of muscular activity remains unchanged. Whenever the triceps reacts on stimulation of this particular cortical focus, its response is immediate (summation time less than one second) whereas the EMG of the biceps appears only after a relatively long latent period. The latter may be greatly reduced by proprioception as fig. 7 indicates, but this reduction is definitely limited. When, as a result of proprioceptive stimulation of the biceps the EMG of the latter is greatly intensified and the activity in the triceps response is suppressed, the EMG of the biceps does not appear immediately (fig. 7, a″, b″) although such a response is readily obtained on stimulation of a more lateral point on the surface of the motor cortex.

The experiment reproduced in fig. 8 concerns likewise a point in the

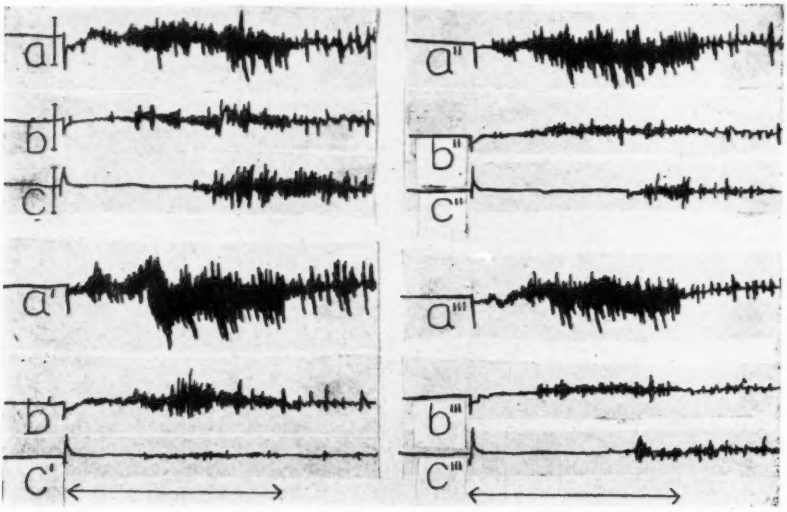

FIG. 8.—Stimulation of site 7 with 2·9 volts for five seconds. Calibration: 150 microvolts; a to a‴ extensor carpi, b to b‴ biceps, c to c‴ triceps. Elbow fixated respectively at 45 degrees and 150 degrees in a to c and a′ to c′; elbow respectively at 45 degrees and 150 degrees in a″ to c″ and a‴ to c‴ but not fixated.

reversal area, but in this case the sequence is not triceps-biceps, as illustrated in fig. 7, but that of biceps-triceps. Moreover, there is no sharp temporal separation between the activity of the two muscles, but rather an overlap since the EMG of the triceps appears during the latter part of the period of stimulation while the EMG of the biceps still continues. Fig. 8 also illustrates that in this case in which an alteration of the angle of the elbow is without effect on the cortically induced muscle activity

when the elbow was not fixed (fig. 8, a″, b″, c″ and a‴, b‴, c‴), fixation of the latter is very effective. Fixation of the elbow at 45 degrees increases the triceps response and fixation at 150 degrees practically abolishes it whereas the biceps response is changed inversely. However, here again the basic pattern noticeable in the biceps-triceps sequence is preserved.

The last experiment illustrating the reactivity of the reversal area under the influence of proprioceptive stimulation shows under control conditions a very slight immediate reaction in the triceps followed by a distinct delayed response in the biceps (fig. 9). This pattern is maintained

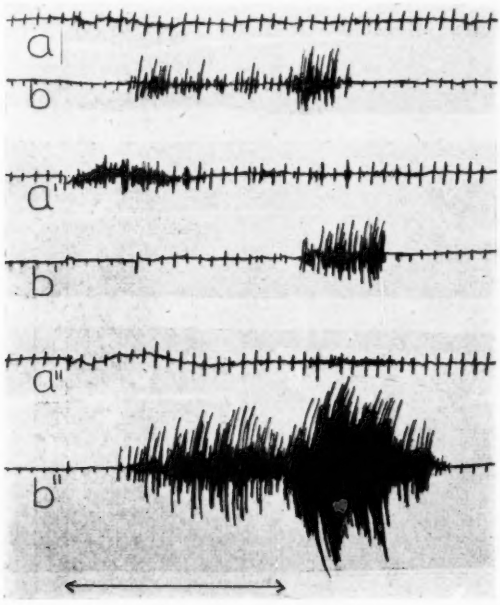

FIG. 9.—Stimulation of site 6 - 7 with 2·3 volts for five seconds. Calibration: 150 microvolts; a to a″ triceps, b to b″ biceps. Elbow at 90 degrees not fixated in a, b, elbow fixated respectively at 45 degrees and 140 degrees in a′ b′ and a″, b″.

under fixation. As a result of fixation of the elbow at 45 degrees the triceps response is greatly intensified as seen by an increase in amplitude and duration of the EMG, whereas the biceps response does not appear at all during the period of stimulation, but shows activity only in the form of an after-discharge. However, under conditions favouring the appearance of biceps activity through proprioception (elbow fixed at 140 degrees) the EMG of the biceps is greatly intensified during and after the period of stimulation. The summation time is likewise shortened but the EMG of the biceps fails to appear immediately on stimulation in spite of the

absence of the triceps response although stimulation of some foci in more laterally located parts of area 4 induces an immediate contraction of the biceps.

Fig. 10 shows records obtained from the lateral (biceps) part of area 4. The triceps showed some tonic activity in this animal. Without

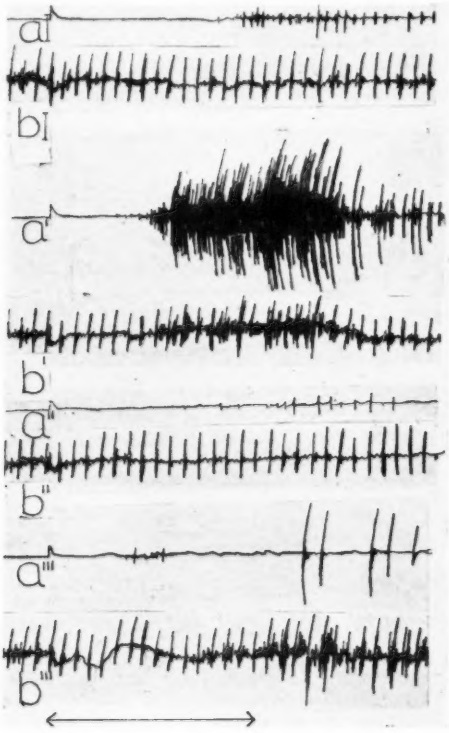

FIG. 10.—Stimulation of site 9 for five seconds. Calibration: 50 microvolts. Intensity of stimulation 4·8 volts in a b to a″ b″. Biceps a to a‴, triceps b to b‴. Elbow at 140 degrees not fixated in a, b, elbow fixated at 140 degrees and wrist fixated in ventroflexion of 100 degrees in a′ b′, elbow and wrist (dorsiflexion), fixated respectively at 65 and 60 degrees in a″, b″, elbow at 65 degrees not fixated but stimulated with 7·3 volts in a‴, b‴.

fixation the response consisted, aside from activity in the carpal muscles (omitted), of a minimal EMG of the biceps which occurred at the end of the stimulatory period and also as an after-discharge, and of an inhibition of the tone of the triceps preceding the EMG of the biceps. Through fixation of the elbow in extension, the responsiveness of the biceps was greatly increased as seen by the increased amplitude of the EMG during

and after the period of stimulation and the shortening of the summation time (cf. also Table I). As in other experiments of this kind the progressive increase in amplitude of the action potentials, signifying a progressive

TABLE I.—INFLUENCE OF PROPRIOCEPTION INDUCED BY FIXATION OF THE ELBOW ON THE SUMMATION TIME OF THE BICEPS.*

Position	*Summation time in seconds*	*Amplitude of EMG*
Elbow 65 degrees, free	4·4	
Elbow 140 degrees, fixed	2·3	
Elbow 65 degrees, fixed	4·0	
Elbow 140 degrees, fixed	1·6	
Elbow 140 degrees, free	3·8	trace
Elbow 140 degrees, fixed	1·0	+++ and after discharge
Elbow 65 degrees, fixed	∞	0
Elbow 140 degrees, fixed	1·3	++ and after discharge

*In both experiments a focus in the lateral biceps area (site 6) was stimulated with 4·8 V, 90/sec. for five seconds.

neuronal recruitment, is clearly seen. However, the activity of the triceps is not markedly altered except for the inhibition of the tone of this muscle which precedes the activity of the biceps and for some co-contraction of the triceps occurring at the height of the activity of the biceps (cf. Bosma and Gellhorn). Fixation of the elbow at an acute angle fails to produce a positive triceps reaction, apparently lengthens the duration of the inhibition of this muscle and abolishes the biceps response. The last record of fig. 10 shows the effect of stimulation with an increased intensity applied to the same cortical site while the elbow was at an angle of 65 degrees without fixation. The responsiveness of the biceps is minimal (fig. 10, a‴, b‴) although a much lesser cortical stimulus under conditions favouring proprioceptive excitation originating in this muscle elicits a very powerful contraction (a′, b′). The triceps shows again inhibition during stimulation followed by some rebound after cessation of the stimulus.

The influence of elbow fixation on the reactivity of a cortical triceps

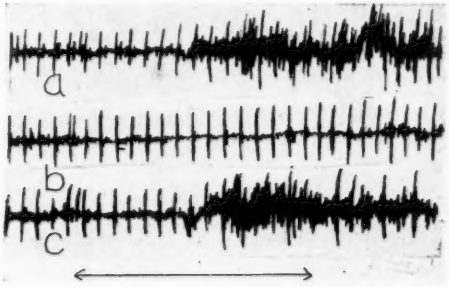

FIG. 11.—Stimulation of site 16 with 3·3 volts for five seconds. EMG of triceps (a to c), elbow fixated at 65 degrees in a and c, and at 140 degrees in b.

point is shown in fig. 11. An increase in triceps potentials occurs when the elbow is fixed at an acute angle but a decrease in the EMG (inhibition of tonic activity existing at rest) is recorded with the elbow fixated at an obtuse angle. No biceps activity occurred during inhibition of the triceps.

Fig. 12 shows the action of proprioception induced by fixation of the

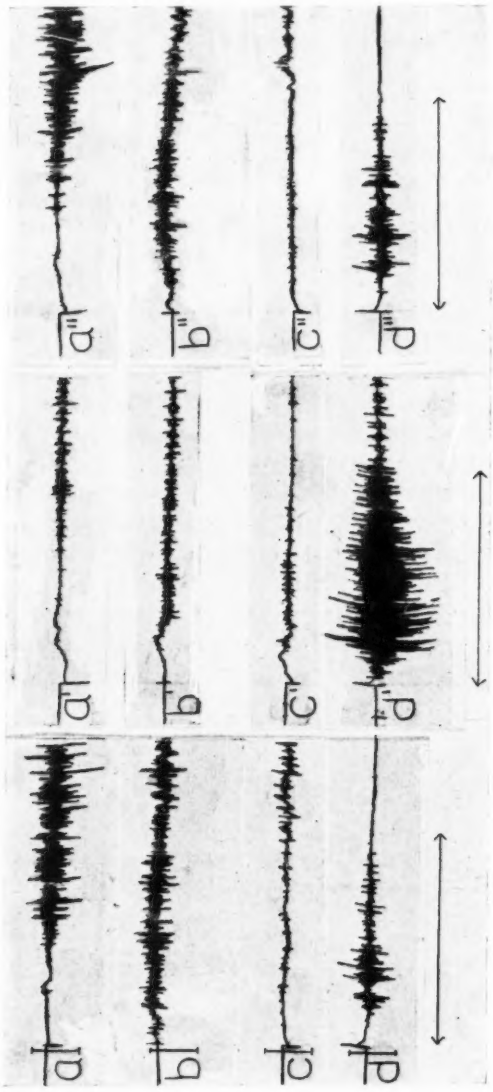

FIG. 12.—Stimulation of site 6 with 2·9 volts for five seconds. Calibration: 150 microvolts; a to a" extensor carpi radialis, b to b" flexor carpi radialis, c to c" biceps, d to d" triceps. Elbow fixated at 150 degrees in a to d and a" to d"; but fixated at 45 degrees in a' to d'.

elbow on a "triceps" point the stimulation of which elicits a distinct action in the carpal muscles as well as triceps. It was pointed out in an earlier study (Bosma and Gellhorn) that the triceps action is associated with that of the flexor and the contraction of the biceps with that of the extensor carpi. This type of pattern is clearly seen in fig. 12 in which the triceps-flexor carpi complex shows activity with a very short summation time, whereas the latter is quite long for the extensor carpi muscle. The study of the records obtained with fixation of the elbow at 150 degrees and 45 degrees shows not only marked differences in triceps activity, which is greatly enhanced at the 45 degrees angle, but also distinct changes in the EMG of the extensor carpi which is known to be a part of the biceps complex[1]. Variations in activity of the extensor carpi bear an inverse relation to that of the triceps. If, as in elbow fixation at 150 degrees the triceps reaction is diminished, that of the extensor carpi is increased, whereas at elbow fixation of 45 degrees the maximal activity of the triceps is accompanied by a minimal reaction of the extensor carpi. The principle of reciprocal innervation appears to be valid also for the carpal component of the biceps complex[2].

III. The organization of the motor cortex in the light of proprioceptive experiments.—A. Experiments on the fore-leg area: In an earlier study (Bosma and Gellhorn) it was shown that, in a monkey anæsthetized with Dial, stimulation of various cortical foci elicited different complex movements which suggested a close functional association of certain muscle groups. Thus it was found by means of EMG records that on stimulation of medial foci of area 4 contraction of the triceps was associated with that of hind-leg muscles (hamstrings), stimulation of lateral foci induced activity in the biceps and extensor carpi muscles and at intermediate sites activity in the triceps was associated with that of the flexor carpi muscle. Between the triceps and the biceps foci was located a zone which on stimulation called forth a biphasic response (consisting of the triceps and biceps complex) which either started with the biceps or with the triceps complex.

The problem to be dealt with in this section is to determine to what extent proprioceptive impulses originating in a certain muscle modify not only its own responsiveness to cortical stimulation, but also that of other muscles associated with it.

Fig. 8 shows that fixation of the elbow at 150 degrees increases not only

[1] The biceps itself does not show any activity during stimulation except for a very slight degree of co-innervation which parallels the degree of activity of the triceps.

[2] The ascending phase of the EMG of the extensor carpi coincides with the declining phase of the EMG of the triceps.

the amplitude of the EMG of the biceps, but also of the extensor carpi which is part of the biceps complex. In another example (fig. 13) the

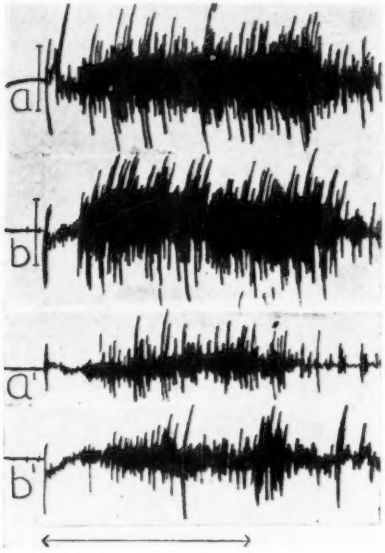

FIG. 13.—Stimulation of site 7 - 8 with 2·9 volts for five seconds. Calibration: 150 microvolts; a, a′ extensor carpi radialis, b, b′ biceps. Elbow fixated respectively at 150 degrees and 30 degrees in a, b and a′ b′.

parallelism in the activity of biceps and extensor carpi is striking. Proprioceptive reinforcement of the biceps by fixation of the elbow at an obtuse angle increases the amplitude of the EMG of biceps and extensor carpi to a similar degree and enhances their after-discharge.

A particularly interesting experiment is reproduced in fig. 14. In the control (elbow not fixated) a typical triceps response associated with that of the carpal muscles is recorded (a″ to d″). Placing the elbow in a position which favours proprioceptive action on the triceps (elbow fixated at 45 degrees, a′ to d′) induces not only an increased triceps response as was to be expected, but also an inhibition of the extensor carpi, the potentials of which are diminished in amplitude and greatly delayed. Obviously proprioceptive facilitation of the triceps is accompanied by an inhibition of the extensor carpi which forms a part of the biceps complex. Conversely, fixation of the elbow at 160 degrees, i.e. in a position favouring proprioception in the biceps, leads to distinct potentials in the biceps which were

previously absent and to a greater amplitude of the EMG of the extensor carpi (fig. 14, a to d)[1].

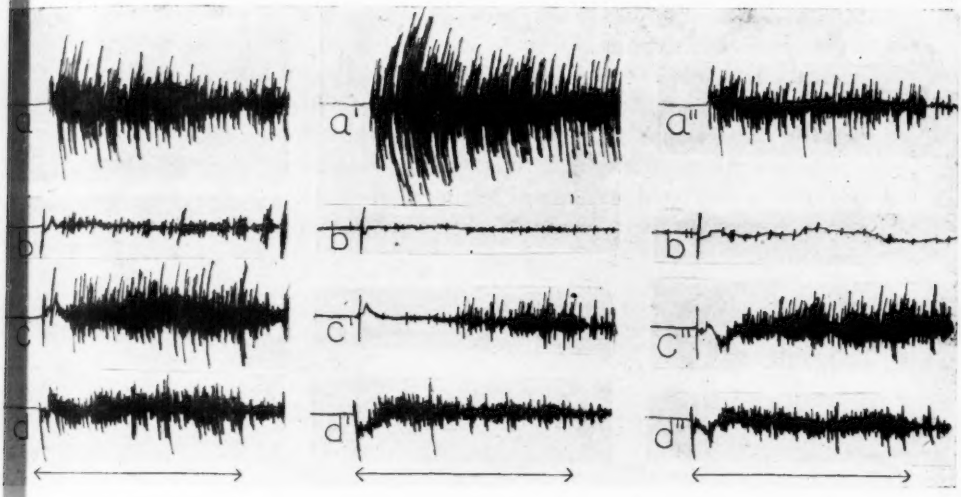

FIG. 14.—Stimulation of site 5 - 6 with 5·5 volts for five seconds; a to a″ triceps, b to b″ biceps, c to c″ extensor carpi, d to d″ flexor carpi. Fixation of elbow at 160 degrees in a to d, fixation of elbow at 45 degrees in a′ to d′, elbow at 75 degrees and not fixated in a″ to d″.

[1] In addition to proprioceptively induced changes in a muscle or muscle complex the rules of co-innervation modify the EMG response. Bosma and Gellhorn showed earlier that considerable activity in an agonist causes co-innervation in the antagonist. This co-innervation is more marked when the biceps complex is activated than when the cortical foci regulating the triceps complex are stimulated. These rules are valid also when the muscle response is increased through proprioceptive impulses while the cortical stimulus remains unchanged. Examples of co-innervation of the triceps when the biceps response was greatly increased under favourable proprioceptive conditions are seen in fig. 10 (a′, b′) while fig. 14 (a′, b′) shows that greatly increased triceps activity may appear without appreciable co-innervation of the biceps. Similar results were obtained with the carpal muscles. If the responsiveness of the extensor carpi is increased, by proper fixation, the effect is apparent not only in the increased amplitude of the potentials of this muscle, but also of the flexor carpi through co-innervation (fig. 15, a″, b″) but in the reverse experiment involving proprioceptive stimulation of the flexor carpi little if any co-innervation occurs (fig. 15, a′, b′).

The rules regulating co-innervation become operative not only when one of the carpal muscles is activated by fixation of the wrist but also when, as a result of elbow fixation, the carpal part of the biceps complex is intensified. Thus, the increased responsiveness of the extensor carpi in turn causes an increased amplitude of the EMG of the flexor carpi (fig. 14, c, d).

It was shown that proprioceptive impulses which increase the reactivity of the biceps are reflected in the strength of the electromyographic response of extensor carpi. A similar influence may also be shown to exist in the reverse direction. Thus, on stimulation of a biceps focus, the response of this muscle may be increased by fixation of the wrist in flexion. This increases the responsiveness of the extensor carpi through proprioception and in addition exerts a facilitatory effect on the biceps (fig. 16). Extension of the wrist does not have this effect.

Proprioceptive influences originating in the triceps may likewise induce not only an increased response of this muscle to cortical stimulation, but also a greater reactivity of the flexor carpi which is part of the triceps

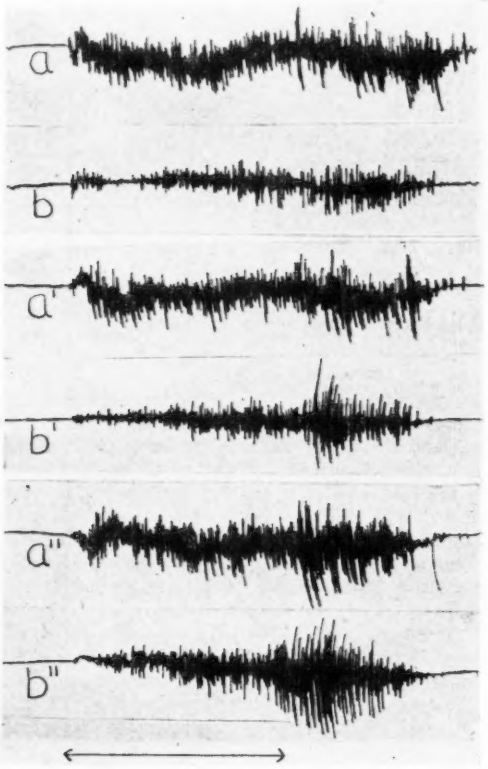

FIG. 15.—Stimulation of site 6 - 7 with 2·3 volts for five seconds; a to a″ extensor carpi radialis, b to b″ flexor carpi radialis. Elbow at 150 degrees not fixated in all experiments; wrist 180 degrees not fixated in a, b, wrist fixated in 35 degrees dorsiflexion in a′, b′ and fixated in 55 degrees ventroflexion in a″, b″.

complex. This is shown in fig. 17 in which under control conditions (elbow at 75 degrees, not fixated) activity appears in triceps and carpal muscles, the flexor carpi showing larger potentials than the extensor carpi while biceps activity is absent. On cortical stimulation while the elbow is fixated at 45 degrees the activity of the triceps is greatly increased as indicated by the more than doubling of the EMG amplitude and marked decrease in the summation time. In addition the flexor carpi shows likewise a greater response. The intimate relation existing between these two muscles is illustrated by the synchrony of the onset of response showing

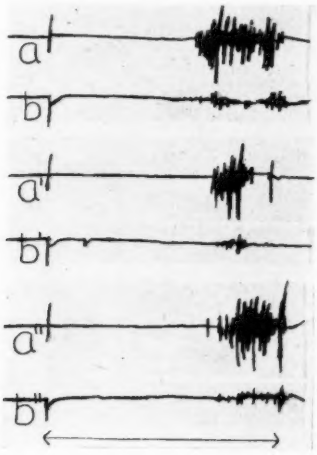

FIG. 16.—Stimulation of site 8 - 38 with 4·8 volts for five seconds; a to a″ biceps, b to b″ triceps. Elbow fixated at 130 degrees in all three experiments, but wrist ventroflexed 90 degrees and fixated in a, b and a″, b″ but not fixated at 180 degrees in a′ b′.

a decrease in summation time in both muscles. In addition, the proprioceptive facilitation of the triceps causes an inhibition of the biceps complex. This appears in fig. 17 in the form of a delay of the EMG of the extensor carpi and a decrease in its amplitude.

B. Experiments on the hind-leg: Although our experiments on muscle combinations of the hind-leg which can be elicited by stimulation of medial sites of area 4 are still incomplete, it was noted that stimulation of the cortex frequently leads to activity of tibial and hamstring muscles. The question arose therefore whether proprioceptive impulses in one of these muscles would also increase the response of the other muscle. Fig. 18 shows that a stimulus which elicits only a trace of a potential in the anterior tibialis when this muscle is shortened through ankle fixation in

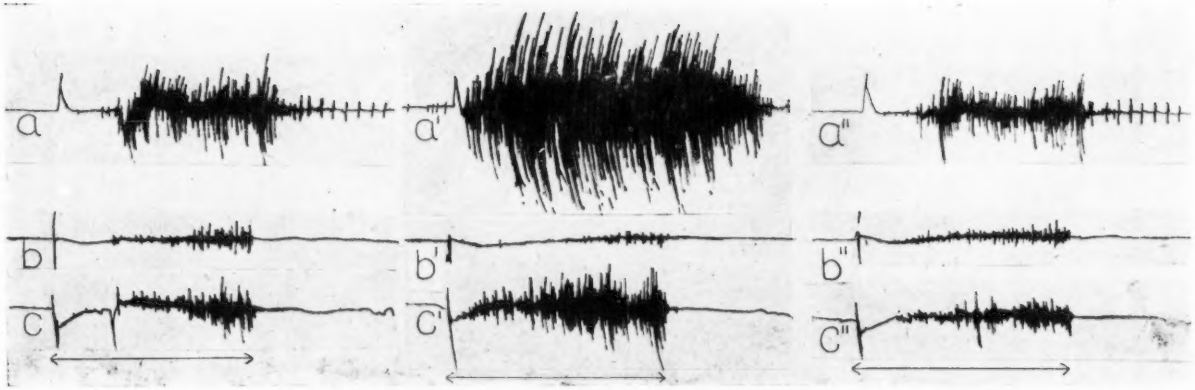

FIG. 17.—Stimulation of site 6 with 2·9 volts for five seconds; a to a″ triceps, b to b″ extensor carpi radialis, c to c″ flexor carpi radialis. Elbow at 75 degrees not fixated in a to c and a″ to c″, but fixated at 45 degrees in a′ to c′.

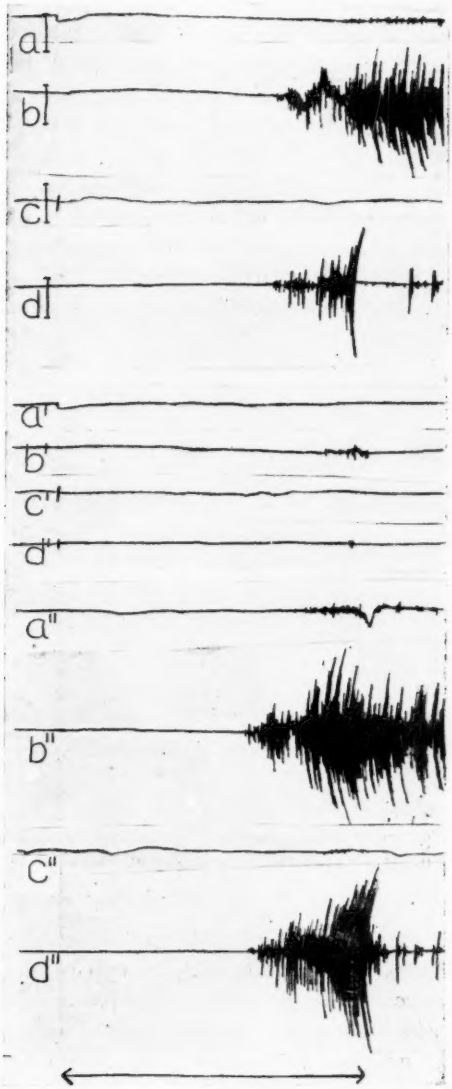

FIG. 18.—Stimulation of site 3 - 13 with 1·9 volts for seven seconds. Calibration: 150 microvolts; a to a″ gastrocnemius, b to b″ tibialis, c to c″ quadriceps, d to d″ hamstrings. Knee at 90 degrees, not fixated in all experiments; ankle fixated at 70 degrees of plantar flexion[1] in a to d and a″ to d″, ankle fixated at 70 degrees of dorsiflexion in a′ to d′.

[1]The angle of plantar flexion or dorsiflexion being 0 when the ankle is 90 degrees.

dorsiflexion becomes a powerful activator of the tibialis when the ankle is fixated in plantar flexion. However, this effect is not restricted to the stretched muscle, but appears also as increased activity in the hamstrings. Further experiments show that proprioceptive impulses act in the opposite direction as well. The comparison of EMGs of tibialis and hamstrings with and without fixation of the knee at an angle of 110 degrees shows clearly (fig. 19) that fixation increases the responsiveness not only of the muscle whose contraction is opposed by the fixation (hamstrings) but also that of the tibialis. If, as a result of proprioception originating in the tibialis or in the hamstrings the responsiveness of the tibialis is increased, it is in most instances accompanied by some co-innervation of the gastrocnemius (figs. 18 and 19). However, the activity of the hamstrings is not accompanied by a co-contraction of the quadriceps.

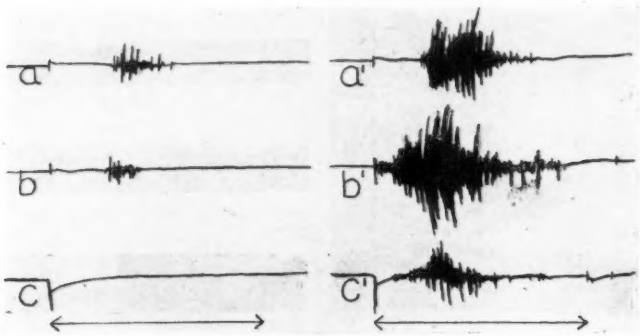

FIG. 19.—Stimulation of site 14 with 6·3 volts for five seconds; a, a′ hamstrings, b, b′ tibialis, c, c′ gastrocnemius. Ankle 100 degrees not fixated in both experiments; knee at 110 degrees not fixated in a to c, but fixated at this angle in a′ to c′.

An attempt was also made to determine whether proprioceptive impulses of the fore-leg could influence the activity of the hind-leg and vice versa, under conditions of cortical stimulation. Medial sites from which the triceps-hamstring complex were elicited were chosen for study. In many instances no effect was seen from one extremity to the other, but in a few cases these effects were clearly present and reversible. Fig. 20 shows electromyographic records of triceps and hamstrings with and without fixation of the elbow. It is obvious that this fixation increases not only the responsiveness of the triceps, but also that of the hamstrings. It is worthy of note that the pattern of activity which the hamstring potentials reveal in this experiment and which consists of a biphasic response

separated by a period of inactivity is not qualitatively but only quantitatively altered. This biphasic response is still present when as a result of proprioceptive impulses originating in the triceps the hamstring response

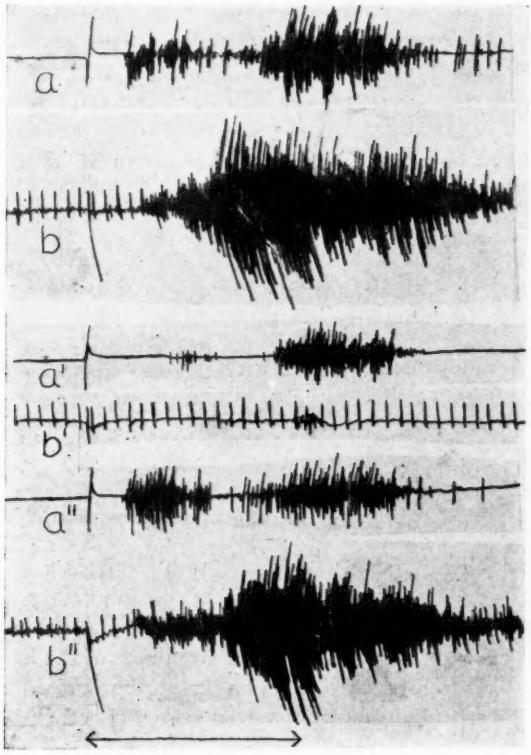

FIG. 20.—Stimulation of site 4 with 3·3 volts for five seconds; a to a″ hamstrings, b to b″ triceps. Elbow fixated at 45 degrees in a, b and a″, b″ but not fixated at 110 degrees in a′ b′. In all three experiments the hind-leg is in the same position (hip 90 degrees, knee and ankle 100 degrees) and is not fixated.

increases, but the separation of the two phases is less distinct (fig. 20, a, b) or shortened (a″, b″ of this figure).

DISCUSSION.

Cooper and Creed showed that contraction of the hamstrings caused by stimulation of appropriate motor roots induced a relaxation of the tone of the quadriceps of the decerebrate cat. The effect of a given stimulus was greater while the knee was extended than when it was in flexion.

These experiments were interpreted to mean that tension rather than change in length of muscle tends to set up proprioceptive impulses which may reflexly inhibit the tone of the antagonist. In another series of experiments these authors studied also the excitatory action of proprioceptive impulses and observed that contraction of the hamstrings or of the anterior tibial muscle induced by stimulation of their motor roots caused a reflex contraction of the sartorius muscle. Here again the effect increased when the indirectly stimulated muscles were prevented from shortening. Cooper and Creed's work showing the excitatory and inhibitory action of proprioceptive impulses on spinal reflexes has been extended in the present study to movements resulting from cortical excitation.

Taking the experimental results of this and the preceding paper into account, it may be said that proprioceptive impulses increase the responsiveness to cortical stimulation of those muscles in which the impulses originate as a result of passive stretching and active tension, and that the effect is directly related to these two factors. Thus, it was found that the cortically induced triceps response is inversely related to the angle of the elbow and that at a given angle of the elbow, the effect increases when through fixation additional tension is developed in the muscle. As the experiments reported in this paper show the latter factor is far more effective than the former.

The amplitude of the EMG chosen as an indicator of the muscle response was found in a recent study from this laboratory to be directly related to the number of discharging units. Factors such as load which modify tension were without effect on the amplitude of the EMG in experiments with indirect supramaximal stimulation, but caused the EMG to increase when cortical stimulation was employed (Loofbourrow). It may therefore be concluded that proprioceptive impulses which are most effectively set up in conditions involving isometric contraction of muscles (fixation of a joint) greatly intensify responsiveness to stimulation of the motor cortex by recruiting more motor units.

The magnitude of this intensification is considerable since subthreshold cortical stimulation may be made effective by bringing proprioceptive impulses into play whereas often even a considerable increase in stimulus intensity fails to cause the same motor effect in the absence of such facilitatory proprioceptive impulses (fig. 10). This proprioceptive recruitment is seen in the greater rapidity with which the peak amplitude of the EMG is reached as well as in its absolute magnitude. It is responsible also for the production and intensification of an after-discharge (fig. 11). Finally, it accounts for the reduction in summation time frequently

encountered under favourable proprioceptive conditions (Table I and figs. 2, 5, 8, and 20).

In addition, it was shown that the effect of proprioception originating in a muscle by fixation during stimulation of a cortical focus is not restricted to this muscle, but appears in certain other muscles which according to our earlier studies (Bosma and Gellhorn, 1947) are functionally closely associated with the former. Proprioception from the biceps was seen to increase the cortically induced response of the extensor carpi and proprioception from the triceps enhanced, although to a lesser extent, the EMG of the flexor carpi resulting from cortical stimulation. Moreover, these proprioceptive impulses operate also in the reverse direction, i.e. from the carpal muscles to biceps and triceps, but here again the specific association (biceps with extensor carpi and triceps with flexor carpi) is preserved. As was to be expected the fixation of the elbow at an obtuse angle is more effective in increasing the biceps response to cortical stimulation than is fixation of the wrist in ventroflexion and vice versa. Similar results were obtained with cortical foci producing activity in the hamstrings – tibial and in the triceps – hamstrings complex. The general organization of the motor cortex shows multiplicity of muscle representation in individual foci and confirms the earlier work from this laboratory (Murphy and Gellhorn, 1945; Bosma and Gellhorn, 1947). It should be emphasized that this is not due to excessive stimulation since, as the figures of this paper illustrate, as low an intensity as 1·9 volts (cf. figs. 5 and 18) may cause activity in the thigh muscles and in the tibialis anticus.[1]

The fact that intensification of proprioceptive impulses through fixation of joints of the fore- or hind-leg may bring into appearance activity in certain muscles which is absent in the control experiment not involving fixation poses this question: is the organization of the motor cortex as disclosed by the study of EMGs resulting from cortical stimulation with threshold or slightly suprathreshold stimuli different from that seen in our earlier work in which proprioceptive factors played only a minimal rôle. The answer is definitely negative. As the focus of cortical stimulation shifts from medial to more lateral parts of area 4, the myograms which show at first responses in several muscles of the hind-leg, particularly hamstrings and tibialis, pass over into records of hamstrings and triceps responses while still more laterally the myograms are confined to the fore-leg muscles. The cortical representation of various fore-leg muscles is similar to that described by Bosma and Gellhorn. As a matter

[1]The same holds true for foci of the fore-leg muscles (cf. the illustrations of this paper). Most of the experiments reported in this paper were performed with discharges of about 2 to 3 volts. Rasmussen and Penfield obtained with similar voltage evidence of multiple representation of muscles of the extremities in man.

of fact, perhaps the most significant finding established by the present investigation is the persistence of the pattern of movement characteristic of certain foci of area 4, under conditions which through proprioceptive impulses lead to quantitatively altered muscular responses. This is particularly evident from the study of those cortical areas which give rise to phasic movements. If a cortical stimulus elicits flexion of the elbow followed by extension of this joint, the intensity of the two components may be greatly varied by proper fixation of the elbow, but in no instance was a reversal of the movement accomplished. This is in agreement with the fact that the sequence in phasic movement is not determined by the intensity with which the individual muscles react. Thus it was seen that in the sequence: quadriceps – hamstrings the former showed by far the weaker EMG and similar statements applied frequently to the biceps – triceps and triceps – biceps phasic movement.

The statement made above that proprioceptive impulses modify the response of a given focus only quantitatively but not qualitatively requires some further comment. As has been pointed out earlier a muscle may respond under conditions of proprioceptive facilitation to a cortical stimulus which is infraliminal in the absence of proprioceptive impulses. But the qualifying statement must be added that this is true only for those foci which even in the absence of proprioception are capable[1] of eliciting a contraction in this particular muscle. Consequently facilitation of the biceps muscle remains without influence on a focus in the medial part of area 4 which elicits a contraction in hamstrings and tibial muscles.

It is of interest to compare the influence of increased proprioceptive impulses on the motor cortex with that of pain impulses originating in muscle (by injection of hypertonic NaCl solution) or in other structures (sciatic or brachial plexus). Pain impulses lead to unspecific facilitation of the motor system activated by cortical stimulation since the effect does not seem to be restricted to any particular part.[2] Many muscles not responding under control conditions including those of the extremities ipsilateral to the stimulated cortex are called into action as a result of nociceptive impulses (Gellhorn and Thompson, 1944), whereas the proprioceptive impulses studied in this paper have a specific effect restricted to cortically organized muscle complexes. The question of whether or not proprioceptive impulses, which persist for long periods of time under pathological conditions (muscle contracture), show fundamentally different effects is under investigation at the present time.

[1] i.e. when stimulated with threshold or suprathreshold discharges.

[2] This work was based on experiments on cats only. It remains to be seen whether more restricted nociceptive effects can be obtained in the monkey by the use of carefully graded nociceptive stimuli.

Since proprioception alters the response of the motor cortex to electrical stimuli within wide limits, considerable experimental material was obtained on agonist-antagonist relationships at different degrees of activity. It was shown in earlier studies that with increasing intensity of cortical stimulation (Bosma and Gellhorn, 1945) reciprocal innervation is converted into co-contraction. This applies to experiments involving increasing stress under conditions of voluntary movement (Gellhorn, 1947). The question arose, therefore, whether with increased amplitude of EMG resulting from proprioceptive recruitment while a given stimulus is applied to the cortex, co-innervation would increase in a way similar to that seen when the cortex is stimulated with increasing intensity. The experiments reported in this paper show that this is the case. In fact, the co-innervation appearing as the result of greater proprioceptive action shows all the characteristics described earlier, i.e. increasing activity of the biceps complex (biceps and extensor carpi) has a greater tendency to call forth activity in triceps and flexor carpi in the form of a co-contraction than vice versa (cf. figs. 14 and 15). It was noted also that optimal proprioceptive impulses set up by a cortically induced contraction of the wrist muscles by appropriate fixation increase the EMG response of the extensor carpi more than that of the flexor carpi.

In agreement with the well-known fact that proprioceptive reflexes are accompanied by inhibition of the antagonist, observations were made in this study which likewise show the presence of inhibition. If a cortical focus is chosen which activates antagonistic pairs of muscles, such as biceps and triceps or hamstrings and quadriceps, increased activation of one muscle through interaction of proprioceptive impulses and cortical stimulation is accompanied by diminished and often delayed activity[1] in its antagonist, as numerous figures of this paper illustrate. However, if, e.g., the action of cortical stimulation on triceps and biceps at elbow fixation at 45 degrees and 150 degrees is recorded and if it is found that triceps activity is increased at elbow 45 degrees and diminished at elbow 150 degrees while the reverse holds for the biceps, the case for inhibition is not clearly established because the length of each muscle is different in the two positions and the conditions of proprioceptive reinforcements are thereby greatly altered. However, as was discussed earlier, a series of observations was made showing that proprioceptive reinforcement of upper arm muscles specifically altered the reactivity of certain carpal muscles. This is particularly clearly established for the triceps since alterations in the activity of the triceps or triceps complex (triceps plus

[1]As fig. 9 indicates it may appear as after-discharge only. This phenomenon is obviously related to the observation of Murphy and Gellhorn that at minimal intensity of cortical stimulation the response appears after cessation of stimulation.

flexor carpi) induce little if any co-innervation. Figs. 12, 14 and 17 show that when the elbow is fixated at an acute angle, the increased response of the triceps is accompanied by a diminished and delayed response in the carpal component of the biceps complex (extensor carpi). Since the wrist is kept in the same position while the elbow angle is altered, the change in reactivity of carpal muscles cannot be due to alterations in the intensity of proprioceptive impulses originating in these muscles. These experiments confirm our earlier observations on the validity of the Sherringtonian principle of reciprocal innervation for muscle complexes such as the triceps–flexor carpi versus the biceps–extensor carpi complex and extend them for conditions in which the EMG is modified by proprioception.

Experiments which are being performed at the present time suggest that the general results reported in this paper are valid also for extrapyramidal cortical areas.

Since it has been found that suitable proprioceptive stimuli greatly increase the cortically induced motor response it is suggested that the mapping of a cortical area prior to its complete removal for physiological and surgical purposes be carried out by means of EMGs while the joints are rigidly held at an acute and an obtuse angle.

Finally, it is suggested that in the performance of exercise and "re-education" in cases involving lesions of the central nervous system, the results of this and a related study (Gellhorn, 1947) be taken into account.

Summary

Experiments are reported on monkeys in which the effect of proprioceptive impulses originating in muscles under condition of temporary fixation of one or more joints is studied on the reactivity of the motor cortex to electric stimulation. Electromyograms recorded simultaneously from four muscles are used as indicators of this reactivity. The results are as follows:

(1) Fixation of a muscle at increased length (e.g. fixation of the elbow at an obtuse angle for the biceps) greatly increases the response of this muscle to stimulation if the proper cortical focus is chosen. This effect is largely due to impulses set up while the muscle develops tension isometrically.

(2) In addition, proprioceptive impulses thus induced become effective, although to a lesser extent, in those muscles with which the proprioceptively excited muscle forms specific functional associations described in an earlier paper. For instance, proprioception originating in the biceps increases also the reactivity of the extensor carpi to cortical stimulation: similar relations exist between triceps and flexor carpi, triceps and ham-

strings, and hamstrings and anterior tibial muscle. It was shown also that this effect occurs in the opposite direction within these complexes. For example, fixation of the wrist in ventroflexion increases the reactivity to cortical stimulation not only of the extensor carpi but also of the biceps muscle.

(3) These effects seem to be based on the interaction of proprioceptive impulses with those elicited by cortical stimulation, resulting in an increased number of discharging motor units. This interpretation is suggested by the decreased summation time, the greater and more rapidly increasing amplitude of the EMGs and, occasionally, by the increased after-discharge.

(4) Proprioceptive reinforcement of a muscle to cortical stimulation is shown to be accompanied by increased inhibition of the antagonistic muscle complex.

(5) Co-innervation (co-contraction) results not only from increased intensity of cortical stimulation as was shown earlier, but also from increased responsiveness of a muscle due to the interaction of a weak cortical stimulus with strong proprioceptive impulses. The rules of co-innervation are also valid for these specific conditions.

(6) The organization of the motor cortex with respect to the multiplicity of representation is confirmed in experiments involving proprioceptive interaction with weak cortical stimuli. Moreover, it is shown that the effects of proprioceptive reinforcement of cortically induced movements depend on the neuronal composition of the stimulated cortical focus. Fixation of the elbow at an acute angle, e.g., will greatly increase the amplitude of the triceps response if a cortical site is stimulated which gives rise to a contraction of the triceps or has the potentiality of evoking a triceps response. Consequently, cortical sub-threshold stimulation may become effective under favourable proprioceptive conditions. Depending on the cortical focus chosen for stimulation, the same proprioceptive condition (elbow fixation at an acute angle) may result in an increased triceps response combined with increased reactivity of the hamstrings (focus more medial), or with that of the flexor carpi (focus more lateral). If a still more lateral focus is used, the fixation of the elbow becomes ineffective for the triceps since this muscle is no longer activated from the cortex. Application of this principle to other muscles studied in this paper confirms the diagram of cortical representation of Bosma and Gellhorn.

(7) It is suggested, first, that proprioceptive reinforcement in conjunction with a weak cortical stimulus be used in order to map completely the cortical foci area in which a certain muscle or group of muscles is represented; second, that the mechanism of the proprioceptive-cortical

facilitation be utilized in therapeutic procedures (exercise, "re-education") in patients with central lesions.

I am glad to acknowledge my indebtedness to Dr. J. F. Bosma and Mr. H. M. Ballin.

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Addendum

Since this paper has been submitted for publication several investigations dealing with proprioception were performed in this laboratory. Cf. Loofbourrow, G. N., and Gellhorn, E. (1948) *Am. J. Physiol.*, **154**, 433, "Proprioceptively induced reflexes"; Hyde, J., and Gellhorn, E. (1949) *Am. J. Physiol.*, in Press, "The influence of deafferentation on stimulation of the motor cortex"; Gay, J. R., and Gellhorn, E. (1949) *Prov. Soc. Exp. Biol. and Med.*, in Press, "Cortical projection of proprioception in the cat and monkey"; Gellhorn, E., Hyde, J., and Gay, J. R. (1949) *Arch. Internat. Pharmacodyn.*, in Press, "Proprioception and convulsions".

THE SIGNIFICANCE OF TINEL'S SIGN IN PERIPHERAL NERVE INJURIES[1]

BY

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Introduction

In 1915 Jules Tinel first described the "signe de fourmillent" as a tingling sensation produced in the cutaneous distribution of the nerve by percussion or compression of the nerve trunk over the site of the newly formed axis cylinders. Although Tinel was the first to attempt an interpretation of the phenomenon he was by no means the first to record it. It was described by Letiévant in 1873, later by Head and Rivers (1905), and by Trotter and Davies (1909 and 1913). This sign had been familiar to neurologists, prior to Tinel's application of it to the diagnosis of peripheral nerve injuries, as the phenomenon of peripheral reference described by Head and more fully by Trotter and Davies, and later by Boring (1916).

Both the immediate and the remote consequences of the publication of Tinel's paper were rather unfortunate. The immediate result was that undue emphasis was laid on the favourable prognosis afforded by the sign, which later led to an almost complete repudiation when it was found, in practice, to be fallible in this respect. Tinel was careful to draw a distinction between "formication" produced by pressure over a nerve and referred distally, and the "sensibility of nerve on pressure" found in neuralgic irritations, which is always a local sensation. The former sign, he stated, is pathognomonic of the presence of young axis cylinders in the process of regeneration and its occurrence below the lesion warrants the conclusion that there is more or less complete regeneration. He further believed that the total absence of the sign below the lesion is likewise pathognomonic of a complete interruption if "sufficient time has elapsed since injury for regeneration of axis cylinders to have occurred."

[1]Much of the substance of this paper was given in a communication to the Society of British Neurological Surgeons in February 1946 under the Title "A Revaluation of Tinel's Sign." Publication has been withheld so that a long-term assessment of recovery could be made.

Macdonald (1918), appealing for conservatism in the treatment of nerve injuries, strongly endorsed Tinel's views. Burrow and Carter (1918) advocated delay in exploring the nerve lesion as long as Tinel's sign was progressive below the lesion. Danforth (1919), Thorburn (1920), and Forester-Brown (1920) all found Tinel's sign of considerable value. Forester-Brown noted its absence in a few cases but in the others observed it to descend more or less regularly. Danforth considered it to be "a reasonable assurance of physiological continuity." However, doubt was already rife in America; Stookey (1919) showed that a positive Tinel's sign was not necessarily indicative of an incomplete lesion; Elsberg and Woods (1919) considered it to be of doubtful value largely on the basis that it was found to be present in macroscopically total lesions. Pollock and Davies (1933) found it to be absent in 7 out of 50 recovering cases and present in some form in all but 7 out of 50 complete interruptions. Coleman (1944) writes ". . . in World War I . . . too much reliance was placed on Tinel's sign which was considered by some to possess a high degree of infallibility. Time and time again patients with Tinel's sign . . . were found at operation to have separated bulbous nerve ends without the slightest possibility of regeneration." Seddon, Medawar and Smith (1943) found it irregular and unreliable as a guide to the rate of regeneration in man in all but a small series of cases of nerve suture where it was said to advance with notable regularity. Nathan and Rennie (1946) did much towards rescuing the sign from rapidly approaching oblivion and placing it in its proper perspective as a rough but valuable clinical guide but they also endorsed its unreliability in that they found it absent in 18 per cent of the lesions in continuity in which regeneration was occurring and in 21 per cent of cases after suture. In no case did they find a positive sign present in a nerve lesion showing anatomical division. They were, however, the first to record the essential feature of Tinel's sign—whether or not it is progressive. Woodhall and Lyons (1946) found Tinel's sign entirely absent in 115 cases out of 456. Spurling and Woodhall (1946) found it absent in 8 out of 59 cases of late primary suture.

In general then the pendulum of esteem has swung, between the two world wars, from one extreme to the other, so that at the present time, although Tinel's sign still maintains its custom-honoured position in most general textbooks, it is considered by the majority of neurologists and neurosurgeons to be of negligible value; and indeed it is extremely rare, as Nathan and Rennie observe, to find any mention of it in the notes of many hundreds of cases that one peruses. This unfortunate state of affairs is perhaps the natural consequence of elevating to the status of a sign of regeneration a phenomenon which can be produced in apparently normal sensory or mixed peripheral nerves. Tinel's sign is not specifically

a sign of *regeneration* of nerve fibres but of the condition of exaggerated sensibility of sensory nerve fibres to a mechanical stimulus.[1]

Material

This investigation is based on the findings in 242 nerve lesions seen at Hill End Hospital in the peripheral nerve injury unit during October 1944—July 1946 and, subsequently, at a follow-up clinic at St. Bartholomew's Hospital.

175 cases involving 201 nerve lesions were specifically investigated for Tinel's sign. Table I shows that a large majority resulted from gunshot wounds. Of the total figure 156 were lesions in continuity and 45 cases of complete division.[2]

Of the lesions in continuity 7 were cases of transitory interruption without peripheral degeneration; 149 were cases of physiological interruption with complete peripheral degeneration. Tinel's sign was present in 139 cases of physiological interruption and absent in 10. It was present in 4 cases of transitory interruption and absent in 3. It was present below the lesion before operation in 21 cases of division and absent in 24.

Table I.—Classification and Ætiology of Nerve Lesions Considered in This Paper

Type of lesion	*No. of cases*	*Classification*	*G.S.W.*	*Fracture*	*Laceration*	*Traction*	*Ischæmic*	*Total No. of cases*	*Tinel's sign*	
									Present	*Absent*
Continuity	156	Transitory interruption	5	–	–	2	–	7	4	3
		Physiological interruption	132	6	5	4	2	149	139	10
Complete division	45	Division	39	1	5	–	–	45	21	24

[1]The phenomenon of peripheral reference which is the salient feature of Tinel's sign is found to occur in a variety of conditions. Percussion of normal nerve produces a tingling sensation referred to the appropriate peripheral zone, as for example the commonplace occurrence of "knocking the funny-bone." A similar sensation can be produced by other forms of stimulation of normal nerve, for example, by percutaneous electrical stimulation. The peripheral reference produced by percussion of a pathological nerve differs only from that produced in a normal nerve by the ease with which it can be evoked and by the tendency towards persistence of the sensation for a short time after removal of the stimulus. A peripherally referred tingling sensation which may be elicited in the autonomous zone of the nerve by a variety of mechanical stimuli is invariably present in the early stages of cutaneous sensory recovery. A similar sensation is found in neuritic conditions and may be produced by a mechanical stimulus of any part of the nerve concerned. It is also a symptom of some causalgic states and is apparently of spontaneous origin, although, as Kinnier Wilson points out, dysæsthesiæ—the subjective element of sensation being implicit in the term—are, in a large number of instances, aggravated by extrinsic stimuli. For the purposes of this paper the designation "Tinel's sign" is limited to the syndrome found in peripheral nerve injuries on percussion of the nerve, and it is not used as a synonym of peripheral reference in its widest sense. The limited application of the term is artificial and may be confusing, but greater confusion might ensue if its use were avoided in this paper.

[2]In the majority of cases discussed in this paper the lesions were of a mixed pathology and "pure" cases of one or other syndrome were rarely found. In these cases classification has been made in accordance with their predominating features.

Method of Examination

Tinel's sign can be elicited by light percussion or compression of the nerve trunk through the intervening soft tissues. The detection of the sign depends entirely on the subjective reactions of the patient, a disadvantage which may be partially mitigated by ensuring that the test is carried out in the comfortable and private surroundings that are an essential of any examination of the sensory system. The interpretation of the sign demands, ideally, a determination of the lowest point reached by the fine regenerating axis cylinders. In practice, it appears likely that the detection of the lower limit of these axons would lag behind the experimental equivalent—the direct pinch method employed by Gutmann, Guttmann, Medawar and Young (1942). If such a difference exists it would be justifiable to object to the use of the sign for quantitative studies of nerve regeneration rates, but in clinical use such a difference would hardly be significant.

After the patient has been asked to close his eyes, the nerve is lightly percussed with a reflex hammer throughout its length. The percussion is begun at the lowest point of the autonomous zone concerned and carried up towards the lesion, the hammer striking the part at approximately 0·5 cm. intervals. Various precautions are taken to minimize the risk of false readings and these are noted below:

(*a*) *Direction.*—The percussion is always commenced distally and continued proximally to avoid the error due to the persistence of tingling once it has commenced.

(*b*) *Strength of percussion.*—This is varied according to the estimated thickness of the intervening structures.

(*c*) *Distribution of tingling.*—The patient is asked to indicate the exact peripheral area where tingling is perceived and thus confusion due to percussion of adjacent nerves or spread from one nerve to another is avoided.

(*d*) *Transmission of impulse.*—The examiner's free hand "blocks" the limb proximal to the point of stimulation and is moved upwards in advance of the percussion hammer. The flat of the hand may conveniently be used to do this. This manœuvre reduces the possibility of spread of the percussion wave to a higher level with a consequently fallacious reading.

(*e*) *Check readings.*—Several check readings of the lower limit of Tinel's sign are taken. A quarter of a minute interval between readings allows any previously aroused tingling to settle.

(*f*) *Measurements.*—Measurements are taken with a flexible centimetre rule from an appropriate bony point.

Tinel's Sign in the Syndrome of Transitory Interruption

Out of 156 cases of lesions in continuity only 7 cases showed the features of a transitory interruption. Out of these 7 a dissociated lesion occurred only in 3 cases. In none of these 3 cases was there any loss of either proprioceptive or cutaneous sensibility nor was there a Tinel's sign *at any time* during observation. In the remaining 4 cases transitory interruption of the nerve was associated with some temporary sensory disturbance and, although a descending Tinel's sign was present at some period in these 4 cases, it was never very evident and it was assumed that it represented the presence of a small number of immature axis cylinders that had undergone Wallerian degeneration and were in the process of regenerating. 3 of the cases with a transient sensory disturbance exhibited severe causalgic symptoms. All 3 patients complained of a spontaneous

sensation of "pins and needles" which could also be elicited by tapping over the site of the lesions.

It is of interest to observe that in those cases that showed an incomplete sensory loss the retained sensation was abnormal. Pain had a low threshold and a markedly intense response but was not associated with peripheral reference; until the arrival of regenerating axis cylinders in the cutaneous area of the nerve had occurred the sensation of peripherally referred tingling was totally absent from the pain response.

Tinel's Sign in the Syndrome of Physiological Interruption

There were 149 cases in the series which showed, predominantly, the features of this syndrome. Tinel's sign was present at some time in all but 10 of this group. The cases in which the sign was absent could be satisfactorily explained thus: 5 cases—injury to nerves having no components subserving cutaneous sensation; 5 cases—injury to nerves which were relatively inaccessible to external stimuli.

Of the 5 cases in which motor fibres only were injured, 4 were injuries to the posterior interosseus nerve and one was an injury to the motor root of T 1.

Tinel's Sign in the Syndrome of Division

45 cases of division were investigated for Tinel's sign both before and after operation. Tinel's sign was found pre-operatively, below the lesion, in 21 of these cases and was absent in 17. To allow for the error that might arise as a result of the vibration of the percussion wave being transmitted through soft tissues to the site of the lesion, no sign was recorded as positive unless it was found more than 10 cm. below the lesion. In 7 cases a positive sign was found less than 10 cm. below the lesion and these cases were therefore excluded.

Both macroscopic examination at the time of operation and subsequent microscopic examination showed that in the group of 21 cases where Tinel's sign was present 14 of the lesions were manifest anatomical gaps. In 2 cases in this group the size of the gap was not recorded and in 2 others gaps of 10 cm. were found. Of the remaining 10 cases in the group the size of the gaps between the cut ends ranged from 1 cm. to 3·5 cm. with a mean at 1·8 cm. The remaining 7 were cases of division without actual anatomical separation of the nerve, the appearance of continuity being preserved by an intact epineurium. 2 cases with a pre-operative Tinel's sign below the level of the lesion were found at operation to have gaps of 10 cm. between the neuroma and the glioma. In both cases a narrow band of fibrous tissue was found bridging the gap but it was not possible to demonstrate the presence of either axis cylinders or of neural supporting tissue by histological section. In one case (fig. 1) which at operation was

found to have a gap of 1 cm. between the neuroma and the glioma the presence of many fine regenerating axis cylinders was demonstrated, indicating some degree of spontaneous reunion of the nerve ends.

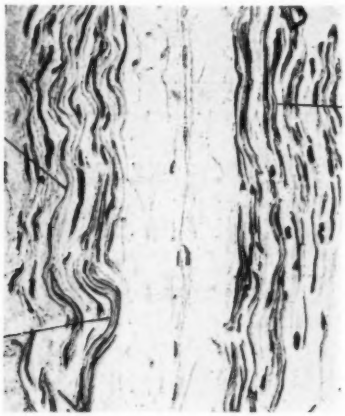

FIG. 1

L.S. nerve trunk (lateral popliteal) below a complete division with an anatomical gap of 1 cm. shows the normal appearance of Wallerian degeneration. The presence of fine regenerating axis cylinders (ax) indicates that some spontaneous reunion of nerve stumps has occurred. There is an empty neurilemmal sheath in the centre of the field. ×300. Holmes' silver method.

Histological examination of the excised neuromata in 6 out of the 8 cases where Tinel's sign was progressive pre-operatively showed that the lesions were incomplete divisions, although with the exception of a positive Tinel's sign they presented the clinical picture of complete division. Fine and, for the most part, non-myelinated axis cylinders were seen passing from the proximal end through into the distal end (figs. 2 and 3). In the remaining 2 cases histological section was not carried out but macroscopic evidence of continuity was present.

The average size of the gap between the neuromata in the 17 cases in which Tinel's sign was absent pre-operatively was 4·3 cm.

In this group of 45 cases of clinically complete lesions, Tinel's sign was found well below the lesion in 21 cases. In only 8 was it progressive and in only 2 out of these 8 was the descent both rapid and progressive. It was possible to demonstrate histologically in 6 of these lesions with a progressive sign that axis cylinders were passing through the lesion in neurilemmal channels. This observation forms a reasonable basis for the explanation of the presence of a Tinel's sign in the nerve trunk below an otherwise complete division.

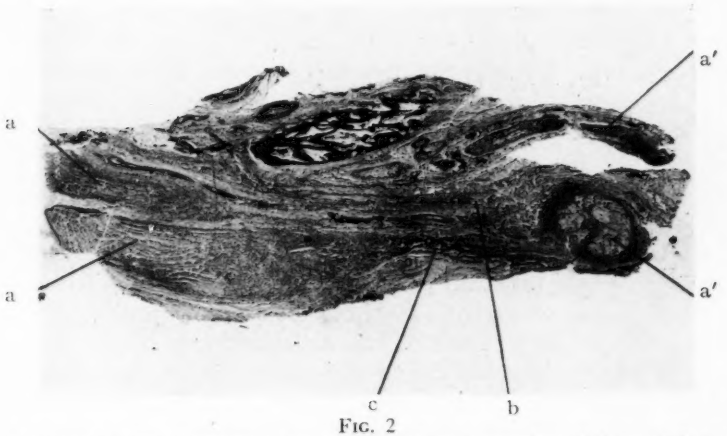

FIG. 2

L.S. Radial nerve neuroma. An example of an incomplete division with a progressive Tinel's sign. Nerve bundles at a and a′ contain myelinated and non-myelinated axis cylinders. Even in region of densest scar (b) isolated and disorientated nerve bundles are found. Narrow band of communicating nerve bundles at c. (Hæmatoxylin and eosin. ×4.)

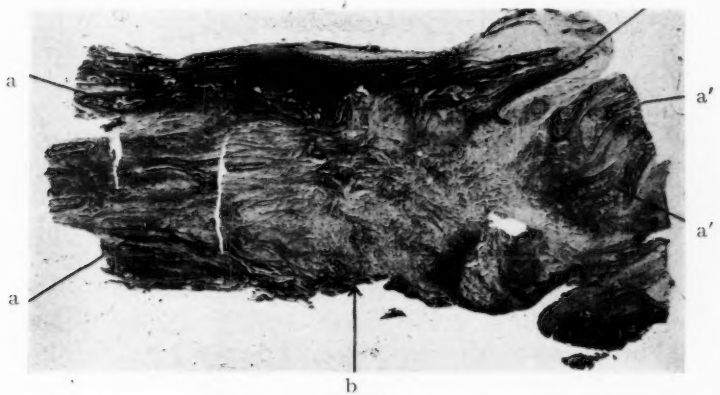

FIG. 3

L.S. Sciatic nerve neuroma. An example of an incomplete division with a progressive Tinel's sign. Nerve bundles at a and a′ contain myelinated and non-myelinated axis cylinders. Dense collagen in which few recognizable neural elements are present extends over 4/5 diameter of nerve at level marked b. (Hæmatoxylin and eosin. ×4.)

RATE OF DESCENT IN TINEL'S SIGN

Attempts to estimate regeneration rates in peripheral nerve injuries are fraught with the complicating factors of the haphazard pathology of the lesion and the variables associated with clinical examinations of human

subjects. This last factor is especially true of Tinel's sign which depends largely on the introspective capacity of the patient. Therefore an expression of rate can only refer to one particular lesion, or, at the best, to a particular group of lesions if their pathology is sufficiently similar. The pathology of the lesions of peripheral nerve injuries is, in the large proportion of cases that recover spontaneously, an unknown factor. The pathology of cases that have been sutured is also far from being standardized dependent as it is on the extent of the original injury and on the technique of operation. In none of these cases is sufficient data available to permit use of the pathology as the standard to which the rate may be related. However, a rough estimate of the pathology can be reached retrospectively by assessing the ultimate degree of recovery shown by the nerve. A complete recovery is dependent, in lesions in continuity, on a minimal degree of intraneural and extraneural disturbance and, in sutures, on the perfect restoration of the intraneural pattern. Recovery then is proportionately related to the severity of the lesion if such factors as age, level, and alterations in the peripheral condition of the muscles, &c., are excluded: therefore cases in which a similar degree of recovery has occurred may be assumed to have had the same gross pathology at the site of injury.

The time of the first appearance of axis cylinders in the nerve trunk below the lesion will depend on certain factors which have not up to now been satisfactorily elucidated. The work of Cajal (1928) and others has shown that a retrograde degeneration in the proximal stump occurs but it seems unlikely that it would account entirely for the relatively long periods of delay that have been found experimentally. One of the most important factors is the effect on growth of the axis cylinders of the formation of fibrous tissue at the site of the lesion. The length of the "scar delay" is probably dependent on the arrangement of the fibrous tissue as well as on its extent: the length of this delay will be reflected in the rate of descent of Tinel's sign which is computed by dividing the distance travelled by the regenerating nerve fibres by the number of days from the date of injury or suture. A long scar delay at the lesion will give a low mean rate and a short scar delay a high mean rate.

The rates given in Table II are of cases in which the degree of recovery was classified as good[1]; this is a fairly broad grouping and within these

[1]Grading of Recovery

Poor.—Motor: Perceptible contraction in proximal muscles (M1). *Sensory:* Recovery of deep cutaneous pain in autonomous zone (S1).

Moderate.—Motor: Return of perceptible contraction in proximal and distal muscles (M2). *Sensory:* Return of some degree of superficial cutaneous pain and touch in autonomous zone (S2).

Good.—Motor: Return of function in proximal and distal muscles to such an

limits the gross pathology of the lesions is assumed to have been similar. Thus the figures in Table II represent the mean rate of descent of Tinel's sign in those cases in which a good recovery occurred.

TABLE II.—RATES OF DESCENT IN MILLIMETRES PER DAY, ± STANDARD DEVIATIONS, AFTER SUTURE AND AFTER PHYSIOLOGICAL INTERRUPTION

	Spontaneous recovery			*After suture*		
	Total No. of cases	*Rate of descent mm./day*	*No. of cases*	*Rate of descent mm./day*	*No. of cases*
Ulnar ..	13	2·8 ± 0·7	5	3·0 ± 0·5	8
Radial ..	14	2·2 ± 0·4	8	2·1 ± 0·4	6
Sciatic ..	13	2·5 ± 0·9	9	2·8 ± 0·3	4
Median ..	8	2·3 ± 0·0	2	1·8 ± 0·5	6

It will be seen in Table II that for the ulnar, radial and sciatic nerves the rate of descent following suture lies between 2·1 and 3 mm. per day and that of the spontaneous recovery group between 2·2 and 2·8 mm. per day. In the ulnar and sciatic groups the rate following suture is slightly higher than it is in the spontaneous recovery group. In the radial nerve group the reverse is true. The rate for spontaneously recovering median nerves in 2 cases was 2·3 mm. per day and following suture was 1·8. Possibly this latter reading is a reflection of the operative difficulties of suture of the median nerve in the region of the elbow as in all these cases the lesions were at or about that level.

In the small number of cases where the readings were numerous enough to justify consideration, a progressive diminution in rate of advance was found. In figs. 4 and 5 the growth curves for 2 of these cases are shown. The regressions were calculated and fitted in the normal manner; an exponential relationship giving a closer fit than a linear one. Serial readings were obtained in 17 other cases but although on examination of the figures they showed the same tendency to fall off progressively, too much reliance cannot be placed on them owing to the unavoidable meagreness of the observations.

In spite of the fact that the curves shown in figs. 4 and 5 are representative only of the progress of fibres which are probably among the fastest growing, it seems probable that Tinel's sign gives a truer picture of the rate of growth of human nerves than that given by estimations of motor or sensory recovery where the maturation time, necessary for functional

extent that all important muscles act against resistance and synergic and isolated movements are possible (M3, M4, M5). *Sensory:* Return of superficial cutaneous pain and touch with or without return of two point discrimination (S3, S4).

The figures in brackets represent the equivalent categories recommended in the Medical Research Council Memorandum (1943).

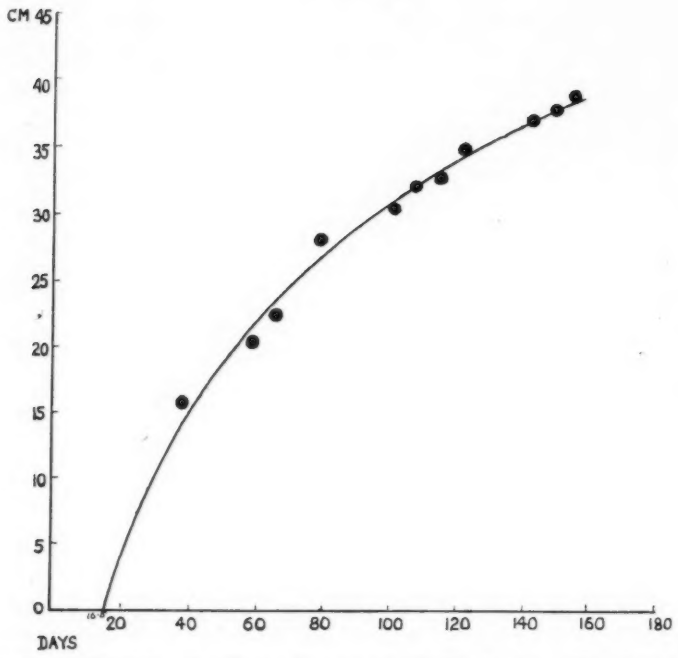

FIG. 4 (*Case* PNI/202).—Graph showing descent of Tinel's sign. The "scar delay" is estimated at 16·5 days.

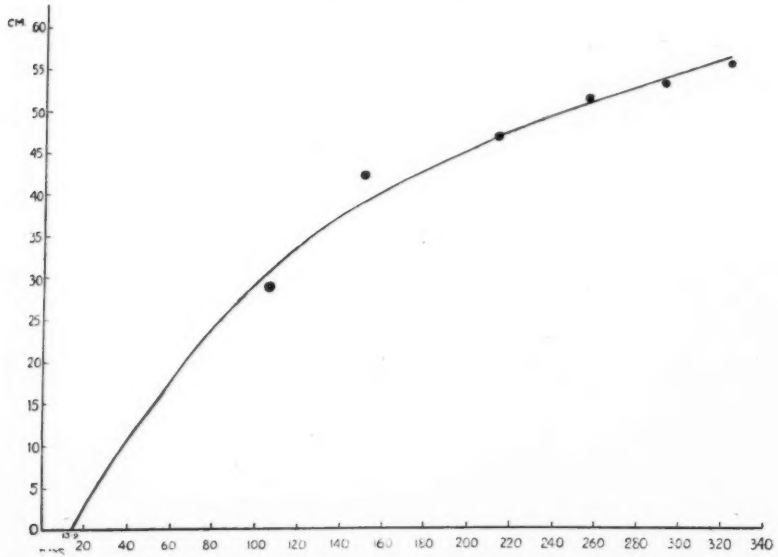

FIG. 5 (*Case* PNI/87).—Graph showing descent of Tinel's sign. The "scar delay" is estimated at 13·9 days.

completion, is unknown. The work of Gutmann *et al.* (1942) using the experimental equivalent of Tinel's sign—the direct pinch method—does not support the hypothesis that the time and distance relationship is exponential but as Seddon (1943) pointed out this may be due to the length of the rabbit's limb which gives no time for the falling off to become apparent. Thus their picture is one of a linear relationship that is seen in the early stages of regeneration in human nerves.

It will be seen that the regression lines in figs. 4 and 5 intersect the time-base, the distance between this point and 0 days representing the delay at the site of the lesion before the regenerating fibres appear in the distal trunk. This figure was found to be 16·5 days in case PNI 202 and 13·9 days in case PNI 87. These figures compare favourably with the experimental findings of Gutmann *et al.* (1942) who observed that the period of delay differed only slightly after crushing and after suture. Both of these cases showed eventually excellent neurological recovery. Case PNI 202 was a physiological interruption of the left ulnar nerve following fracture of the medial epicondyle in a boy aged 14. Recovery was complete at the end of nine months. Individual movements of the ulnar-supplied intrinsics had returned and two-point discrimination was present (MRC grading M4, S4). Case PNI 87 was a suture of the lateral popliteal nerve in the thigh under ideal conditions. At the end of three years the patient had regained almost full voluntary power in all muscles except the extensor digitorum brevis and had had recovery of pain and touch sensibility which was free of "over-response" (MRC grading M4, S3).

The opportunity for frequent and regular readings of level in PNI 202 makes this case a valuable one in illustrating the progress of Tinel's sign in a "pure" case of physiological interruption.

Fate of Tinel's Sign

The following figures relate to the fading and disappearance of Tinel's sign over a period of three and a half years in 80 cases. The findings are considerably at variance with the orderly manner described by Tinel in which the disappearance above occurred *pari passu* with the progress below. Only one case was seen where anything like this orderliness of behaviour occurred (Case PNI 202, *vide supra*).

Table III shows the state of Tinel's sign in 48 cases seen between two and a half years to three and a half years after suture or injury. The sign had already disappeared in 9 cases (19 per cent). Of the remaining 39 cases, the sign disappeared in a further 9 during this period. At the end of three and a half years the sign could still be elicited in 30 cases although in 20 (42 per cent) it was in the process of fading.

TABLE III.—STATE OF TINEL'S SIGN IN 48 CASES SEEN TWO AND A HALF TO THREE AND A HALF YEARS AFTER SUTURE OR INJURY

		Suture	*Physiological interruption*	*No. of cases*
Absent .. 19%		6	3	9
Disappears .. 19%		3	6	9
	Persists though fading	11	9	20
Persists .. 62%	Persists unchanged	3	7	10
		23	25	48

In 80 per cent of cases Tinel's sign commenced to fade centrifugally but in 20 per cent fading commenced in a centripetal direction. After centrifugal fading had occurred in the peripheral course of the nerve a strongly positive Tinel's sign invariably persisted at the neuroma and for a few centimetres on either side of it.

After correlation of the degree of sensory recovery with the ultimate fate of the sign it was found that the earlier the sign disappeared the better was the ultimate recovery. It was also found that early fading and disappearance was rather more frequently associated with suture than with cases of physiological interruption though the difference was hardly significant.

TINEL'S SIGN IN THE AUTONOMOUS ZONE OF THE NERVE

Following suture of a peripheral nerve the descent of Tinel's sign may be traced by percussion throughout the length of the nerve below the lesion and into the autonomous zone, through which it continues to progress, though apparently at a less rapid rate, until the extremities of the zone are reached. It may also be elicited equally well in the autonomous zone by digital compression. Subsequently a peripherally referred tingling sensation (hereafter referred to as PRT), said to be of the same quality as that elicited by percussion and compression (i.e. Tinel's sign), may be produced by pricking the skin with a needle. In a large number of cases examined by the writer this PRT has been present in every case in which recovery of cutaneous sensation was occurring by a process of regeneration. It was never found in the absence of regeneration. PRT was never found in advance of Tinel's sign nor was it ever found to be present unless there had been a Tinel's sign at some time. Furthermore PRT was never found in incomplete lesions with partial sparing of sensation until the regeneration of the previously degenerated fibres had occurred. These findings suggest that Tinel's sign and the PRT found during recovery of cutaneous sensation are merely different instances of the same phenomenon.

The tingling sensation produced by the needle stimulus is both intensified and peripherally referred and is completely unlocalized by the patient.

The sensation is usually referred to the most distal part of the autonomous zone but the occurrence of retrograde and lateral reference is quite common. The same quality of sensation is produced whether the blunt or the sharp end of the needle is used and the patient is unable to differentiate between them. The tingling sensation may be described as unpleasant but the patient will seldom admit that the sensation is actually painful. The adjectives most commonly used to describe it are "peculiar" or "curious" and sometimes "uncomfortable." The next stage in the recovery of the pain response is the occurrence of a local sensation in addition to the peripheral response. This appears at first to be the appreciation of a sensation of pressure from the needle which serves roughly to localize the stimulus, the PRT remaining unaltered. This ability to "localize" stimuli appears to be associated with recovery of deep sensibility. The next stage is the appreciation of the sharpness of the stimulus which now produces local pain. This pain response which has a high threshold appears to be superimposed on the PRT and patients have no difficulty in distinguishing between the pain and the tingling, the latter sensation being felt following the pain with a slight delay between the two. As the threshold becomes more normal the quality of the pain response is found to be hypoalgesic as compared with the other side. A hyperalgesic response may occur but it appears to be found most frequently in "low" injuries or sutures especially those at the wrist. A possible explanation may lie in the fact that in low injuries a large number of regenerating fibres will arrive in the cutaneous zone at much the same time producing a condition similar to that found in the skin following a partial lesion where sparing of a large proportion of the sensory fibres is frequently associated with a *hyperalgesic* state.

The PRT elicited by a needle may persist when the tingling produced by percussion and compression has entirely disappeared from the hand. It is too early to comment on the ultimate fate of this PRT in the series of cases under discussion, except to say that in a small series of cases of median and ulnar nerve sutures which have been carefully followed through all stages of their sensory recovery the PRT still persists in 15 after two and a half years and has entirely disappeared in 5 leaving a residual state of hypoalgesia.

Painful stimuli are not the only variety that produce the sensation of PRT. Perception of light touch with a "von Frey hair" is interpreted in this manner and the light brushing of hairy skin produces an intense tingling sensation which differs from the tingling evoked by pulling on a single hair with a pair of fine forceps, both quantitatively and in its characteristics of reference. The same effect may be elicited from hairless skin when it is lightly brushed with the fingers and may occur even in the

absence of any demonstrable recovery of light touch to a Von Frey hair stimulus.

The phenomenon of peripheral reference is not shown in partial lesions where there has been some sparing of sensation. In a small series of 8 cases where there was residual sensation following injury to the nerve the character of the pain response was hyperalgesic in 6 cases and hypoalgesic in 2 cases. In the hyperalgesic group the response was abnormal and diffuse but peripheral reference of tingling was totally absent. This hyperalgesia was apparently similar in its subjective characteristics to the pain referred to by Head, Rivers and Sherren (1905) as occurring in the "intermediate zone" and by Trotter and Davies (1909) and Boring (1916), as occurring in a patchy distribution in the anæsthetic area two to six weeks after division of the nerve; and by Weddell, Sinclair and Feindel (1948) as occurring in association with the histological picture of "isolation" of pain fibres in the subepidermal layer of the skin.

Discussion

Owing to the status of Hill End Hospital in relation to war casualties who formed the main bulk of this series there were no opportunities for seeing early cases and consequently no observations could be made on the first appearance of Tinel's sign below the lesion. The observations of Tinel, Dustin and others suggest that the sign cannot be elicited before the fourth week after suture or injury. From Boring's minute description of his own experimentally divided cutaneous nerve one can estimate that his Tinel's sign could have been elicited at about the twentieth day. In our own cases Tinel's sign was found at some distance down the nerve by the sixth week. In animal experimental work, Gutmann *et al.* (1942) identified the presence of axon tips in the distal stump 7·3 days after suture and 5·2 days after crush. These findings suggest that if suitable means could be devised Tinel's sign could be elicited much earlier than the fourth week given by Tinel. Prior to the appearance of a Tinel's sign in the course of the nerve a positive sign is found at the neuroma. Sharpey-Schaefer (1929), after an experimental crush of his own digital nerve, found that "before many days stroking over and beyond the neuroma elicited a tingling sensation referred towards the periphery." Boring observed this sensation on the ninth day after section and suture on stretching his arm. This sensibility of the neuroma which appears early and persists late (Tinel's sign at the neuroma persisted in 60 per cent of cases where it had disappeared from the rest of the nerve at the end of three and a half years) is extremely valuable in localizing the site of injury. Gentle percussion above the course of the nerve produces a peripheral reference of tingling which becomes more intense as the neuroma is approached and will become

less as the neuroma is passed. Exact localization may be made by percussion from above downwards as well as from below upwards. This is especially valuable where multiple injuries have occurred in the same limb and the actual site of the nerve injury is in doubt.

Tinel's sign is the first evidence of regeneration to occur following a degenerative lesion. It remains the only sign that the lesion is other than a complete interruption until such time as the early signs of motor or sensory recovery occur. The presence of the sign below the level of the lesion is presumptive evidence that regeneration of axis cylinders is occurring. It has been shown experimentally by Gutmann *et al.* (1942) by directly pinching the nerve that the level reached by the most advanced axis cylinders can be accurately estimated. In the series of nerve injuries reported in this paper in which degenerative lesions occurred in mixed nerves recovery of sensory function was preceded by a positive and migratory Tinel's sign *in every case.* The only exceptions to this rule were in 5 cases in which the nerve concerned was relatively inaccessible to stimulus. The corollary that in every case in which Tinel's sign was present subsequent motor or sensory recovery occurred is not, however, true. It has been shown above that Tinel's sign occurs frequently in the presence of anatomical gaps and that it is seldom absent from the case of complete division where the gap is small and the appearance of continuity is maintained by an intact epineurium. In 2 cases with 10 cm. gaps between the divided ends Tinel's sign was present well below the lesion. It is difficult to believe that the fibres responsible for the presence of the sign in these cases bore any relation to the neurilemmal sheath of the distal stump or even the distal stump itself and it must be assumed that they were "casual" fibres which had migrated from the proximal neuroma into the surrounding scar tissue. These instances are examples of the amazing capacity of growth possessed by regenerating fibres in unfavourable surroundings. The possibility that regenerating nervi vasorum may accidentally enter into the peripheral stump as suggested by Holmes and Young (1942) must not be overlooked, but in these circumstances peripheral reference would probably be absent. The frequency with which axis cylinders are found in the peripheral stump distal to small gaps has been shown experimentally by Ramon y Cajal (1928) and Holmes and Young (1942), and clinically by Seddon (1943).

In none of the cases where Tinel's sign was present below a complete division was there any likelihood that spontaneous regeneration would have occurred, had resection and suture not been performed. This appearance of Tinel's sign below a complete division of the nerve has frequently been quoted by clinicians as an instance of its unreliability in diagnosis. However it has been shown above that in none of the cases with large

anatomical gaps was Tinel's sign *progressive* during the period of observation. A single examination therefore will not bring out this important point. A Tinel's sign which progresses steadily towards the periphery is strong evidence of continuity of the nerve, while a Tinel's sign which is non-progressive suggests the presence of a complete interruption.

A progressive Tinel's sign may be found in the presence of an incomplete division where part of the nerve has been divided and there is a lesion in continuity in the remainder. In that part of the nerve where the supporting tissues are intact, downgrowth of axis cylinders will be easy and unimpeded and will give rise to the rapid appearance of a progressive Tinel's sign. This type of incomplete lesion should be suspected where the injury is due to an incised wound rather than to overt mechanical violence which would tend to affect the whole diameter of the nerve. The absence of any evidence of muscle re-innervation, after an appropriate length of time has elapsed, would indicate that the regenerating fibres were insufficient in number and maturation to produce an effect in muscle, and would be a strong point in favour of exploration in spite of a progressive Tinel's sign.

Estimation of the rate of descent of Tinel's sign is extremely valuable in making a rough assessment of the degree of recovery to be expected, and will aid in differentiating between the lesion in continuity which will recover spontaneously and the one which will require resection and suture before any functional recovery can be anticipated. It was found that the rate of descent of Tinel's sign after suture and after physiological interruption differed only slightly. The rate in the ulnar and sciatic groups after suture tended to be more rapid than that occurring after physiological interruption, but in the radial group the rate was found to be much the same in the two types. The rate of descent of Tinel's sign following suture of the median nerve was slow but this may be merely a reflection of the technical difficulties of operation. Rates of the order of 2 to 3 mm. per day were found in this series to be associated with a good recovery and therefore in the absence of any unequivocal evidence to the contrary rates of this order may be accepted as a good prognostic sign. Table IV sets out the available data from clinical observations of rate of descent of Tinel's sign and from the experimental determinations of the rate of advance of axon tips in animals. It will be seen that, except for Dustin's figures, the average rate of 2·6 mm. per day found in all the author's cases considered together is much higher than those recorded by previous observers. It has to be remembered, however, that the author's figures were taken from cases which showed a good recovery only and it is probable that the mean figures quoted by Tinel (1917), Macdonald (1918), and Thorburn and Sargent (1920) were based on a much wider selection. Seddon's (1943)

figure was calculated from the few selected cases of suture in which he found Tinel's sign advancing with notable regularity.

TABLE IV.—SUMMARY OF RATES OF ADVANCE OF AXON TIPS ESTIMATED CLINICALLY (TINEL'S SIGN) AND EXPERIMENTALLY IN ANIMALS

Author	*Date*	*Mean rate mm/day*	*Material*	*Median*	*Radial*	*Ulnar*	*Sciatic*
Tinel	1917	1–2	Clinical No figures	–	–	–	–
Dustin	1917	–	Clinical	2–4·5	4–5	1·5 –2	–
Macdonald ..	1918	1–2	Clinical No figures	–	–	–	–
Thorburn and Sargent	1920	1·0	Clinical No figures	–	–	–	–
Seddon	1943	1·71	Clinical 6 cases	–	–	–	–
Napier	1949	2·6	Clinical 48 cases	S 1·8 A 2·3	2·1 2·2	3·0 2·8	2·8 2·5
Huber	1920	1–2	Experimental No figures				
Cajal	1928	3·5	Experimental				
Gutmann *et al.* ..	1942	S 3·5 C 4·4	Experimental				

S = suture, A = Physiological interruption, and C = experimental crush.

In 15 cases not previously mentioned in this paper where Tinel's sign was present before exploration and suture the mean rate of descent was 1·2 (±0·6) mm. per day. It is interesting to note that the rate of descent is comparable to the figure of 1 mm. per day so often quoted for Tinel's sign. It is quite understandable that, if a rate of 1 mm. per day is accepted as standard, clinicians may easily be misled into believing that a Tinel's sign found in a complete division is proceeding normally. Further observations at regular intervals on these cases would almost certainly reveal that the sign was non-progressive.

SUMMARY OF IMPORTANT FEATURES OF TINEL'S SIGN

(*a*) A Tinel's sign below the lesion is indicative of the presence of regenerating axis cylinders, but by itself is no guide to the condition of the nerve at the site of the lesion, since a positive sign may occur in the presence of an anatomical gap. A positive sign, however, is an indication that degeneration of the whole or of part of the nerve has occurred. Furthermore, the sign may be used to localize the exact site of the injury.

(*b*) The persistent absence of Tinel's sign below the lesion in the presence of motor and sensory paralysis is strongly indicative of a total division of the nerve. Tinel's sign may be absent in the presence of well-established motor and sensory recovery, having faded and disappeared prior to the examination. The persistent absence of a Tinel's sign after

a reasonable time interval, in the presence of an apparently complete motor and sensory paralysis, may be valuable confirmatory evidence in the diagnosis of palsies of functional origin.

(*c*) A *progressive* Tinel's sign is a strong indication that continuity of supporting tissue is present. A progressive sign may occur in a mixed lesion where only a small part of the nerve is in continuity while the remainder has undergone complete division of all neural and supporting tissues. The presence of this type of lesion should be suspected where the injury is the result of an incised wound. Absence of motor recovery at the expected time is a further indication that the lesion is for the main part a complete division. A progressive sign may be found in a lesion where an actual anatomical separation of nerve ends has not occurred, but where a considerable scar tissue barrier is interfering with good spontaneous recovery. Estimation of the rate of descent will indicate the extent of the delay at the site of the lesion and will consequently be a guide to the extent of the scar barrier.

(*d*) Rate of Descent: A rapidly descending Tinel's sign of the order of 2 to 3 mm. per day or more signifies a good prognosis and suggests that the lesion is in continuity and that a minimal degree of intraneural disturbance has occurred. Rates of the order of 1 to 2 mm. per day or less are, similarly, an indication that a good spontaneous recovery is unlikely and that exploration of the nerve should be carried out forthwith.

(*e*) Disappearance of Tinel's sign: An orderly fading above, *pari passu* with progress below, is seldom found but appears to be an excellent prognostic sign. The earlier the disappearance of the sign from above, the better will be the ultimate recovery. Tinel's sign may, however, persist for periods extending beyond three and a half years.

Conclusion

Tinel's sign is a valuable adjunct to the diagnosis and prognosis of peripheral nerve injuries. It is a constant sign and reliable if it is correctly interpreted, but it must be emphasized that its presence is not evidence that functional recovery will necessarily occur; it can only indicate the presence of regenerating sensory fibres. The behaviour of the sensory fibres may be used indirectly to make a rough assessment of the conditions prevailing at the site of the lesion. Tinel's sign may be the only positive evidence of activity of the nerve for many weeks after injury, and the advance information that it affords during this time is extremely valuable in planning the management of the case. A positive, advancing Tinel's sign should never be the criterion for withholding exploration if other evidence points to the presence of complete division. On the other

hand, a negative sign after a suitable time has elapsed is the strongest possible evidence for exploration.

Summary

(1) The history of Tinel's sign is reviewed.

(2) The occurrence and behaviour of Tinel's sign in 209 nerve lesions is considered, and its close relationship to other forms of peripherally referred tingling sensation is illustrated.

(3) The value of the sign in the diagnosis and prognosis of peripheral nerve injuries is discussed and summarized.

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ÉTAT MARBRÉ OF THE THALAMUS FOLLOWING BIRTH INJURY

BY

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ALTHOUGH the subject of birth injury in relation to mental deficiency and cerebral palsy continues to attract attention, there is still a surprising dearth of published cases in which both the pathological and clinical features have been adequately described. The recent contribution of Benda (1945) has, it is true, shown how diverse the cerebral lesions attributed to birth injury may be; yet, even so, the inference that this or that pathological finding is a late sequela of birth injury because of its association with a history of abnormal parturition may fail to carry conviction to a critical reader. It therefore seems of value to describe cases in which pathological features of debatable pathogenesis, such as état marbré of the thalamus, have been found in conjunction with other lesions indisputably the result of vascular damage occurring at birth.

CASE REPORT

V. B., a male idiot, was admitted to Stoke Park Colony when 2 years 8 months old and died at the age of 5 years 3 months.

Family history.—The father and mother are normal and not related by blood. The records state that the mother's uncle was in a mental institution and that the mother's cousin was a certified mental defective.

History before admission.—The patient was the first child of a healthy mother who was 21 years old at the time of his birth. Labour began one month prematurely during an air raid and lasted only one hour and a half. Delivery took place in hospital, the birth-weight being 5 lb. 8 oz. and the records stated that the baby was born with severe blue asphyxia, and did not respond readily to treatment. The infant became very cyanosed at times during the first four days, the hands and feet were seen to be swollen and on the fifth day slight twitchings of the hands and face were noted. A slow improvement in the general condition then set in but feeding remained difficult and vomiting frequently occurred. The mother noted that during the early months the baby tended to hold his arms pressed firmly against his head. Teething started at 8 months but as time passed it was apparent that development was seriously retarded. At the age of 2 years he was unable to raise his head from the pillow and seemed to be blind.

Examination on admission.—At the age of 2 years 8 months the patient was a

well-cared-for, healthy-looking baby weighing 1 st. 8 lb. The head was small, the circumference measuring only 17 in. Abnormal physical signs were confined to the nervous system. The pupils reacted to light but since no interest was taken in objects held before him the reaction to convergence could not be elicited. On ophthalmoscopic examination the discs appeared pale with sharply defined edges, no macular, pigmentary or vascular anomaly being present in the fundus. Conjugate movements of the eyes were inco-ordinate and at rest the left eye squinted outwards. The face lacked the normal play of expression. He was unable to lift up his head and lay with semi-flexed legs and with the arms resting upon the chest, the fists being closed over the thumbs. On stimulation the limbs moved freely, there being considerable activity of a purposeless character, with occasional spreading movements of the fingers but no athetosis. Muscle tone was increased and the tendon-jerks brisk in arms and legs, contracture being present in each tendo Achillis. The abdominal and cremasteric reflexes were not elicited and a bilateral extensor plantar response was present. Modified tonic neck reflexes were obtained, marked flexion of the right lower limb occurring when the head was firmly turned to the left, while on turning the head to the right both legs flexed equally. These movements had no effect on the arms which remained in their position of flexion on the chest.

Subsequent progress.—The child was difficult to feed and could take liquids only very slowly. During the first four months after admission his nurses described several attacks of an apparently convulsive character which were sometimes associated with profuse sweating. He became pale and lay with head retracted, the legs and ankles being rigidly extended with the great toes in the Babinski position, the arms remaining flexed. The pupils were dilated, the eyes fixed in one direction, the mouth closed, the breathing snorting and rapid.

Six months after admission some physical improvement had taken place. He could now raise his head and would attempt to sit up. He was able to grip the examiner's finger and permit himself to be drawn up. Scissor posture of the legs was now a feature of the clinical condition. At the age of 3 years 7 months his accomplishments, as measured by the standards of Gesell, were those of a 7-months-old baby. He did not now seem completely blind and would sometimes fixate moving objects but only with very transitory attention. When 5 years 3 months old he contracted scarlet fever of a mild type and died on the second day of the illness.

Post-mortem examination.—Apart from mild inflammatory changes in trachea and bronchi, no pathological condition was found outside the nervous system. Subsequently histological examination of liver, spleen, kidney, thyroid, suprarenal, testicle and pituitary (weight 0·3 gramme) revealed no significant abnormality.

Pathological examination of the brain.—Macroscopic: The brain weighed 974 grammes of which the cerebellum and brain-stem accounted for 163 grammes. There was no abnormality of convolutional pattern. On coronal section the central white matter of the hemispheres was found to be markedly reduced in extent, the frontal horns of the lateral ventricles being dilated and the corpus callosum abnormally thin (fig. 1). Greyish areas of softening that merged in the left frontal region into obvious cavitation of the tissues were present bilaterally in the white matter adjacent to the outer angle of the lateral ventricle throughout its whole extent exclusive of the temporal horn (fig. 1). In the medial nucleus of each thalamus white streaks suggestive of état marbré were visible to the naked eye.

Microscopic: Blocks of tissue were taken from numerous representative cortical areas, from the basal ganglia, the cerebellum, various levels of the brain-stem and from the optic nerves and chiasma. One eye was embedded in paraffin. Sections were stained by standard methods for nerve cells, neuroglia, myelin, lipoid and connective tissue.

Cerebral cortex: There was no evidence of diffuse cell loss, sclerotic atrophy or

abnormality of myelination in the numerous areas examined. In general the nerve cells appeared somewhat immature and stained feebly with toluidine blue on account of a poverty of Nissl substance.

Centrum semi-ovale: In the paraventricular areas of softening myelinated fibres were absent or markedly thinned (fig. 2 and 3), and had been replaced by dense fibrillary gliosis (fig. 4). Scattered phagocytes containing lipoid or doubly refractile material were found in small numbers in these areas of rarefaction.

Thalami: Sections stained to demonstrate myelin confirmed the naked-eye impression of état marbré in the medial nuclei, dense networks or star-shaped masses of fibres being present in this normally rather poorly myelinated part of the thalamus (figs. 6 and 7). These areas showed, in addition, a very conspicuous loss of nerve cells and some increase in the number of glial nuclei (fig. 5). A moderate proliferation of fibrillary glia was present in the lateral nucleus and internal capsule, but no associated gliosis was found in the areas showing état marbré except to a minor degree around the larger blood vessels.

Visual pathway: The examination of sections taken from the eye which had been embedded in paraffin revealed no abnormality except that the optic papilla contained rather more numerous neuroglial fibrils than is usual (fig. 11). There was, however, no evidence of atrophy in the optic nerves the myelination of which seemed to be intact, though a mild overgrowth of fibrillary neuroglia was also present in them. In the left *optic tract*, close to the chiasma, there was a small area of rarefaction of the myelin sheaths which was accompanied by an increase of neuroglial fibres. The *lateral geniculate bodies* showed considerable loss of nerve cells, mainly in their medial portions, which was evidently the result of partial destruction of the optic radiations by the process of softening observed in the hemispheric white substance.

Brain stem: The pyramidal tracts were small and poorly myelinated, and at medullary level were approximately equivalent in size to those of a normal newly born infant (figs. 8, 9, 10).

The cerebellum, corpus striatum and other parts of the brain that were examined showed no significant pathological change.

Comment

Birth injury had seemed the most probable cause of this infant's physical and mental defects in view of the premature birth, the severe asphyxia and the twitchings of hands and face on the fifth day of life. According to Rydberg (1932) and Benda (1945) minor seizures of this sort in the early neonatal period are especially indicative of cerebral trauma. Furthermore, the slight but definite improvement that had taken place in the general level of accomplishment had enabled one to dismiss from consideration a progressive degeneration of the nervous system such as Krabbe's infantile form of leuco-encephalopathy. Whatever doubts there had been as to pathogenesis were set at rest by the demonstration in the brain of the paraventricular softenings so typical of birth injury. Schwartz (1924, 1927) has recorded several examples of this form of central encephalomalacia which he attributes to intense congestion and circulatory stasis in the anterior terminal and lateral ventricular branches of the great vein of Galen. The latter vessel is vulnerable, as Holland (1922, 1937) has shown, because of its relative mobility compared with that of the sinus

rectus into which it opens, and it is at this point of attachment to the sinus that kinking may occur if the vertical diameter of the skull rises unduly during the process of birth. The thalamus, which is also drained by the great vein of Galen (Alexander, 1942*a*), is another favoured site for the hæmorrhagic or anoxic lesions associated with birth trauma (Wald, 1930), and when one takes into consideration the fact that état marbré of the thalamus is frequently found in conjunction with marbling of the corpus striatum and that the latter is usually caused by birth injury (Norman, 1947), it is difficult to avoid the conclusion that both conditions share a common pathogenesis. There is, then, little reason for supposing that état marbré of the thalamus is a prenatal malformation, as Alexander (1942*b*) has claimed it to be. It must, however, be admitted that the precise mode of origin of the abundant hypermyelinated fibres remains an enigma, though this overgrowth of axis cylinders may perhaps be interpreted with greater plausibility as the consequence of hypertrophy of the collateral branches of injured axons rather than as an example of true regeneration in the central nervous system (Norman, 1937).

Two other features of the case deserve brief comment: the gliosis of the optic papilla and the small size of the pyramidal tracts. The pallor of the optic discs taken in conjunction with the infant's obviously impaired visual powers had led one to believe that optic atrophy was present, similar appearances having been recorded in cases of birth injury by Marburg and Casamajor (1944), Benda (1945) and Marburg (1945). This assumption was, however, belied by the examination of the visual pathways which revealed significant lesions in the optic radiations while the optic nerves remained unaffected apart from a mild gliosis. It is tempting to attribute the pallor of the discs to the unusually numerous glial fibrils found in the optic papilla, this amount of neuroglial proliferation not having been encountered in control sections from other eyes. It is, however, probable that other factors, for example, the degree of vascularity, determine the colour of the discs as seen on ophthalmoscopic examination. Pale optic discs are frequently seen in mental defectives whose visual activity is unimpaired and a pallor suggestive of mild optic atrophy is also often seen in normal babies (Mann). It may be concluded, then, that the appearance of optic atrophy in cases of birth injury may be deceptive, since the blindness may be cerebral and not peripheral and the pallor of the discs may not be due to atrophy of the nerve fibres.

The small size of the pyramidal tracts may be attributed in part to the destruction of some of its component fibres at the time of birth, in part to the stunting effect that extensive lesions are known to exert upon immature structures not directly implicated by the pathological process. It is also possible that the widespread scarring of the central white matter

may have acted as a barrier to the later downgrowth of axons from the motor cortex. The especially severe paresis of the lower limbs in this patient may thus be due either to a failure of the pyramidal fibres to reach the lumbar segments in sufficient numbers, or, alternatively, to the selective destruction of that part of the pyramidal tracts which is derived from the paracentral lobules, for it is these fibres that traverse the paraventricular region of the centrum semi-ovale in their course towards the posterior limb of the internal capsule. It is interesting to note in this connexion that the same set of fibres becomes stretched and atrophied by the expanding ventricle of infantile hydrocephalus, thus giving rise to the paraplegia characteristic of the condition (Yakovlev, 1947).

In conclusion, it is of interest to note that the type of cerebral birth injury described here leads to a clinical picture which has often been regarded as typical of the diplegia of prenatal origin (Collier, 1924; Ford, 1948), namely, the small-headed idiot with a symmetrical paresis affecting the legs more than the arms. Doubtless this clinical impression of a degenerative rather than a traumatic pathogenesis would have been deepened by the finding of apparent optic atrophy, while the observations of Murphy (1947) might have been quoted to imply that the occurrence of premature birth was as much in favour of prenatal malformation as of birth injury. Considerations such as these suggest that opinions concerning the pathogenesis of cerebral diplegia are of little value unless they are based upon correlated clinical and pathological observations.

Summary

An account has been given of the clinical and neuropathological features presented by a 5-year-old male idiot suffering from cerebral diplegia.

The infant was born prematurely and weighed 5½ lb. There was a history of severe asphyxia at the time of birth and twitchings of the hands and face were observed on the fifth day of life. He appeared to be blind and had pale optic discs. Although a slight general improvement was noted in the infant's physical progress he was never able to stand or sit up on account of a symmetrical spastic paresis which affected the legs more than the arms. There were occasional seizures of a tonic type.

Examination of the brain revealed bilateral état marbré of the thalamus and also conspicuous areas of softening in each centrum semi-ovale adjacent to the lateral ventricles. The pyramidal tracts at medullary level were of the size and degree of myelination approximately appropriate to a newly-born infant. The optic radiations and the external geniculate bodies showed partial destruction and there was an apparent increase in the neuroglial fibrils of the optic nerves and optic papilla. It was concluded

that the lesions of the thalami and central white matter, which lay within the drainage area of the great vein of Galen, were late neuropathological sequelæ of birth injury.

LEGENDS FOR PLATES

FIG. 1.—Coronal section of the brain showing dilatation of the lateral ventricles and areas of softening in the adjacent white matter.

FIG. 2.—Right side of the brain, showing absence of myelin in the paraventricular region. Stain as in fig. 3. ×2½. V=lateral ventricle.

FIG. 3.—Left side of the brain, showing absence of myelin in the paraventricular region. Anderson's modification of the Kultschitsky-Pal method. ×3½.

FIG. 4.—Fibrillary gliosis and cavitation in the central white matter adjoining the right lateral ventricle. Victoria blue. ×6.

FIG. 5.—Medial nucleus of the left thalamus showing loss of nerve cells in an area of état marbré. Toluidine blue. ×48.

FIG. 6.—État Marbré of the medial nucleus of the left thalamus. Anderson's modified Kultschitsky-Pal method. ×4½.

FIG. 7.—État Marbré of the medial nucleus of the right thalamus. Stain and magnification as in fig. 6.

FIG. 8.—Medulla showing small, poorly myelinated pyramidal tracts. Anderson's modified Kultschitsky-Pal method. ×2.

FIG. 9.—Normal medulla from a child of 4½ years. Stain and magnification as in fig. 8.

FIG. 10.—Normal medulla from a newly-born infant. Stain and magnification as in fig. 8.

FIG. 11.—Optic papilla showing numerous neuroglial fibrils. Holzer stain. ×80.

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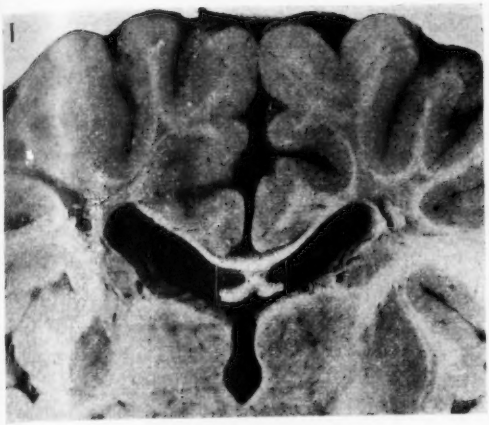
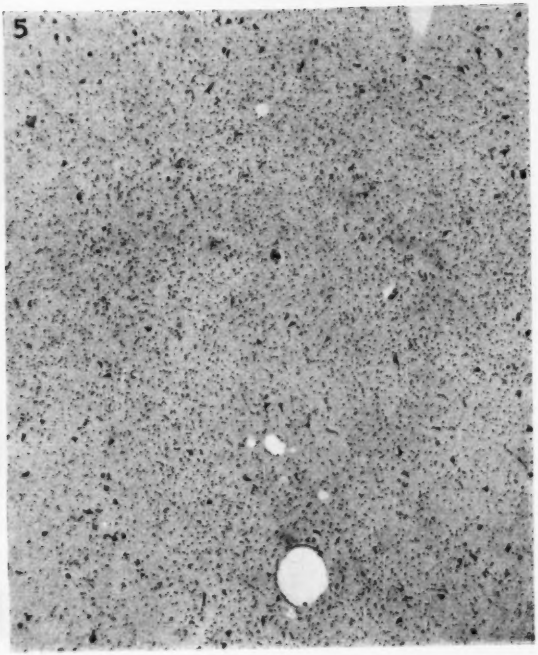
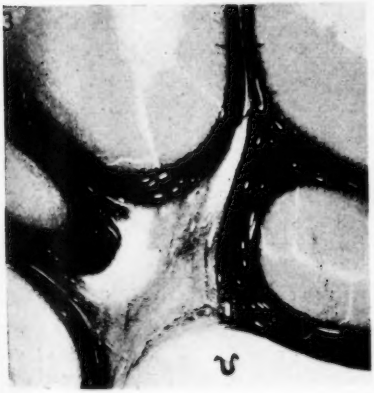
PLATE VI



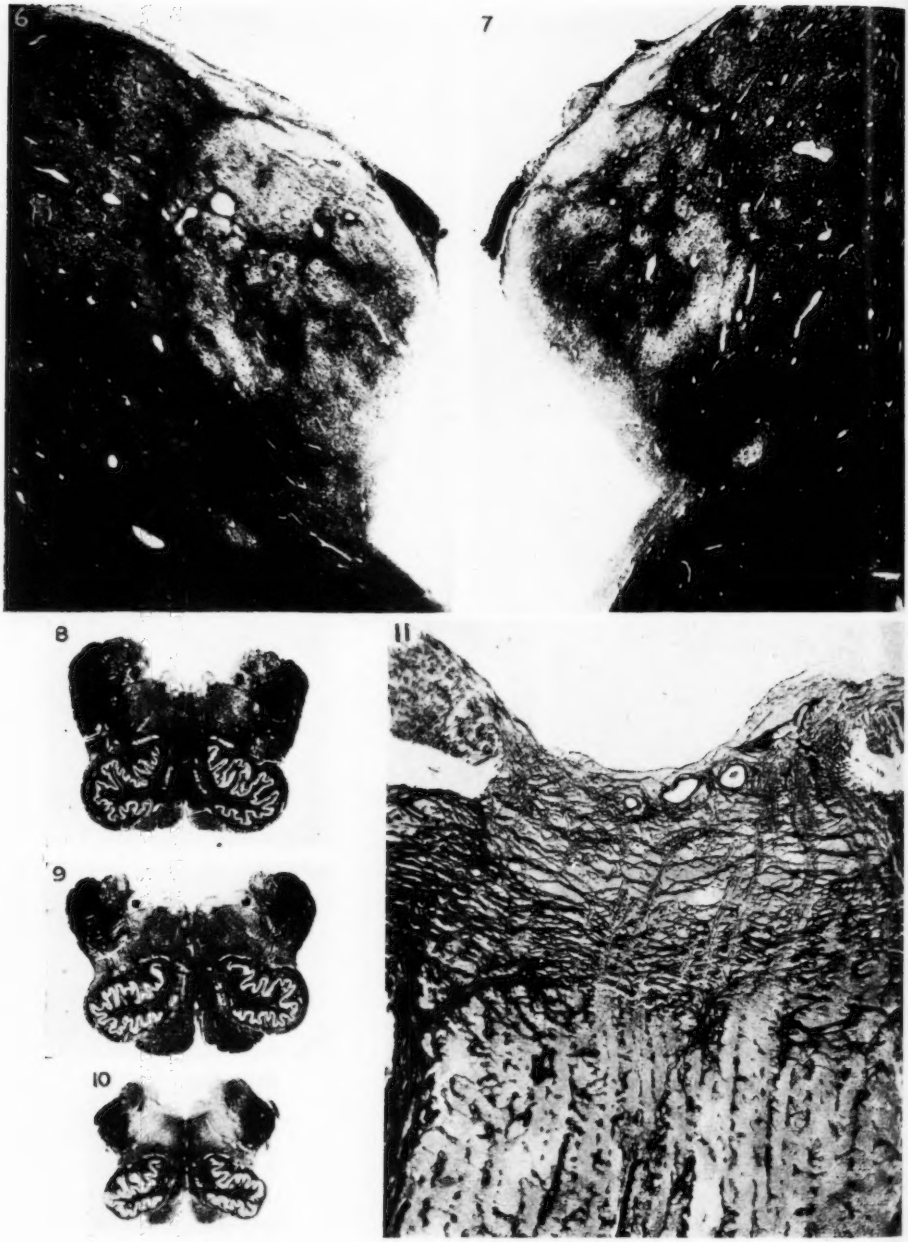




FIGS 1 TO 5.

To illustrate article by R. M. Norman.

PLATE VII



FIGS. 6 TO 11.

To illustrate article by R. M. Norman.

DISORDERS OF THE BODY IMAGE CAUSED BY LESIONS OF THE RIGHT PARIETAL LOBE

BY
MARTIN ROTH
(*From the Hospital for Nervous Diseases, Maida Vale*)

THE concept of the body image as a tridimensional inner diagram each person has of his own body has proved of great value for the understanding of a variety of neurological and psychiatric disorders. The concept originated from the work of Pick (1908) and Head and Holmes (1911). Since Pick described the first case of anosognosia for hemiplegia in 1898, evidence has accumulated to indicate that the parietal lobes are the crucial links in the functional physiological chain concerned with the elaboration of the body image. Lesions of the right parietal lobe produce disordered awareness of the left half of the body, sometimes with delusional confabulations. Lesions of the left parietal lobe produce disorders which are bilateral in distribution. The commonest condition resulting from disease of the major parietal lobe is that described by Gerstmann, in which finger agnosia is usually associated with acalculia, agraphia, loss of right-left discrimination, and constructional apraxia. Gerstmann (1942) believes that finger agnosia is a forme fruste of total autotopagnosia, or inability to identify or indicate any part of the body, and this, in his view, is produced by a lesion involving the "chief representation of the body schema" in the major parietal lobe. This condition is always manifested in a setting of severe intellectual defects, sometimes with clouded consciousness, which obscure the body image disorder and, according to Gerstmann, explain why it is so rarely encountered. Brain (1941) has suggested that the disorder which is obscured in this way by the associated aphasic, apractic and other agnostic symptoms, is a disordered awareness of the right body half, identical with that produced by right hemisphere lesions for the contralateral side. However, very few convincing cases of anosognosia for right hemiplegia, or other delusional beliefs concerning the right half of the body and produced by a lesion in a dominant left hemisphere, have so far been recorded (although the condition may, to a large extent, be diagnosed from the patient's behaviour).

We are mainly concerned here with disorders of the body image pro-

duced by lesions of the right parietal lobe. Two cases are described in this paper. Such disorders are rare and as, in addition, both cases raised some points of interest, it was decided to put them on record.

Case 1.—*History.*—Woman, aged 61, admitted to the hospital for Nervous Diseases, Maida Vale, under the care of Dr. Russell Brain, on May 5, 1944. About 1936 she began to neglect her personal appearance and became careless and untidy in her habits. In 1940, after the death of her husband, she became more careless, slow in her movement, and lacking in initiative. These personal changes progressed slowly, with frequent fluctuations, during the subsequent four years. Seven months before admission the patient noticed weakness and clumsiness in the left upper and lower limbs. There were frequent parasthesiæ in the left hand and foot. The left hand sometimes felt as if it did not belong to her. She tended to drop things she held with it. The left leg dragged slightly on walking. A month later she noticed impairment of vision. She now had throbbing headache commencing over the right eye and spreading over the whole of the head, and also some urgency of micturition. During the month before admission she was incontinent of urine on a few occasions. For six months, while she had been living with her stepson, she had been constantly losing her way about the house, although familiar with it for fifteen years.

Examination between May 5 to 12 gave the following results: She was usually drowsy and a little retarded, but quite well able to co-operation in examination. Head and eyes turned to the right and trunk rotated to the right. Orientation, memory, and retention, within normal limits. Speech normal. Her mood was one of fatuous equanimity. Severe chronic bilateral papillœdema. V.A. 6/18 both eyes. Left homonymous hemianopia with sparing of the maculæ. Pupils normal. Conjugate ocular movement to left poorly sustained. Slight blunting of superficial sensation on left side of face, and marked impairment of tactile localisation and discrimination. Left corneal reflex diminished. Left lower facial weakness. Tongue deviated to right. Marked weakness left upper and lower limbs, with slightly increased tone. Slight impairment of superficial sensation on left, with gross defect in localisation and discrimination and astereognosis in left hand. Postural sense markedly impaired, left side. Inco-ordination of sensory type of left limbs. Abdominal reflexes absent. Bilateral extensor plantar response. All deep reflexes brisk, more so on left side. In walking, head turned to right, left upper limb carried motionless by side and left lower limb dragged. Recognition of objects and colours normal, and performance in matching and sorting tests good. Visual imagery normal.

She was perpetually losing her way about the hospital, going into the wrong room and very often getting into another patient's bed. This disorientation seemed to be due to a failure to take left turnings when necessary. Thus she would walk into the gap between her own and her neighbour's bed and repeatedly chose the latter, which was on her right. She continued to do this after her mistake had been carefully explained to her. A few yards to the left of her bed there was a door opening on to a corridor where the W.C. was situated. Even a week after admission, when wishing to go to the W.C., she would turn right on getting out of bed, walk across the ward and through a door leading on to the verandah, where she wandered about perplexed, until helped by a nurse or patient. Asked to walk along a corridor which turned sharply to the left she would

stop on reaching the bend and, when urged to continue, on each occasion opened a door on her right and walked into the room into which it led.

Tests for motor and ideational apraxis gave normal results, but there was a consistent apraxia for dressing. She always got into difficulties putting on her clothes, often getting them on back to front, and at times omitting to put her left arm into garments.

In constructional tests, simple patterns, such as triangles and squares, were correctly reproduced with matches. More complicated patterns were assembled in a very piecemeal and unorganized sort of way, ending in hopelessly inaccurate reproductions. In free construction, meaningless patterns were arranged. Drawings of a bicycle showed the wheels in different planes and the parts poorly articulated. In drawings from memory, generally, planes were often confused and the left halves incomplete, or even omitted.

Although able to name and indicate parts of her own or the examiner's body, her attitude to her left side was pathological from the time of admission. She kept her eyes turned to the right and tended to ignore events occurring to the left of her. Only with difficulty could she be persuaded to look to the left.

She made no spontaneous complaint of weakness on her left side, but during the first four to five days it was possible to demonstrate her hemiparesis to her, although her emotional reaction to her disability was inadequate. Subsequently, when it was demonstrated to her, she jocularly brushed it aside, saying "It's just a bit of stiffness in it, it will go off." She did complain, however, that she was often unable to find her hand and, on one occasion, she was observed searching for it. Her head and eyes were kept turned to the right and she made groping movements with her right hand towards the left one, not even attempting to orientate herself by finding her shoulder and working her way down. Noticing that she was observed, she said "It feels as if someone had stolen it." On May 12 allæsthesia was observed, painful stimuli to the left upper limb being referred to the right. This finding was recorded frequently during the remainder of the illness.

After this first week she grew apathetic, retarded, doubly incontinent and disorientated for time and place. On May 19 she was transferred to the neurosurgical unit at the Atkinson-Morley Hospital. X-rays of skull showed slight rarefaction of the posterior clinoids. A ventriculogram by Mr. Valentine Logue showed filling of only the left lateral and third ventricles. There was a marked shift to the left and a filling defect on the inner aspect of the body of the left lateral ventricle. The appearances were those of a deeply situated tumour in the parietal region, lying close to the mid-line. It was judged to be inoperable.

She returned to the Maida Vale Hospital on May 21, 1944. Her mood was facile and euphoric; she often wore a silly fatuous smile. She now had a severe retention defect. Within twenty-four hours she had forgotten that she had been to the Atkinson-Morley Hospital. She was disorientated for time and place, often believing herself at home. She never complained about her left side, although weakness of the left upper and lower limbs was now severe. Asked if there was anything wrong with her left arm or leg, she always answered in the negative. On one occasion, however, she replied: "A few days ago that arm was broken, but it is quite all right again, thank you." She thus showed a vague awareness of disease in the past, the gaps in her memory being filled in with a bizarre confabulation. Asked to raise her left arm, she made a few ineffectual attempts at doing so, explaining her failure with "I have been sleeping on it," on one occasion, and on another by saying "It has a cold just now, it will be better presently." This tendency to confabulation was evident only in connexion with her hemiplegia. She steadily became more apathetic, retarded, forgetful, and disorientated, and lost even this vague, fleeting insight into her left-sided disability. After May 30, when asked to raise her left arm, she would raise her right and insist that she was carrying out the request correctly. If any attempt was made to refute her reasoning, she would withdraw from the argument into a sullen, vacant, apathetic state. Retention defect was undoubtedly an important factor in sustaining her delusions at this stage, as she would forget meals or visits from relatives, &c., within minutes. Allæsthesia was frequently elicited, but there was no right-left disorientation. She also showed complete lack of emotional response to painful stimuli on the left side, although her brisk withdrawal response showed that she had perceived them. (Schilder has described this behaviour as "asymbolia" for pain.)

She was sent for a course of deep X-ray treatment on June 19. When next seen on July 14 her condition was essentially unaltered. Subsequently the course was one of rapidly increasing dementia with signs and symptoms of mounting intracranial tension, drowsiness, headache, and progressive impairment of vision. The anosognosia remained essentially unchanged until her death on September 13, 1944.

Post-mortem.—Only the brain could be examined. Inspection of the brain revealed a well-marked cerebello-medullary pressure cone. There was a large bulge in the right parieto-occipital region sharply limited anteriorly by the precentral gyrus and extending posteriorly to the angular gyrus. After hardening, the brain was investigated by means of coronal sections. A section passing through the anterior end of the thalamus showed a small mass, of about 5 mm. in the centrum semi-ovale. 5 mm. posteriorly the tumour was broken up into a 2 mm. mass in the centrum semi-ovale, and several smaller lesions destroying the cortex and underlying white matter of the precentral and postcentral gyri and the lower part of the

superior frontal gyrus. The intersulcal meninges were invaded here as in all subsequent sections. At the level of the mamillary bodies the tumour occupied a wedge-shaped area with its apex about ½ cm. above the roof of the distorted lateral ventricle, limited laterally by the destroyed cortex of the precentral, postcentral and superior frontal gyri, ventrally by the Rolandic fissure (of which the cortical borders were intact) and dorsally by the central sulcus. Sections from the level of the red nucleus to that of the geniculate bodies showed the tumour occupying the same portion of the hemisphere, destroying the lower two-thirds of the precentral and postcentral gyri, most of the supramarginal gyrus and the superior parietal lobule (figs. 1A and 1B). Part of the cortex of the angular gyrus was obliterated

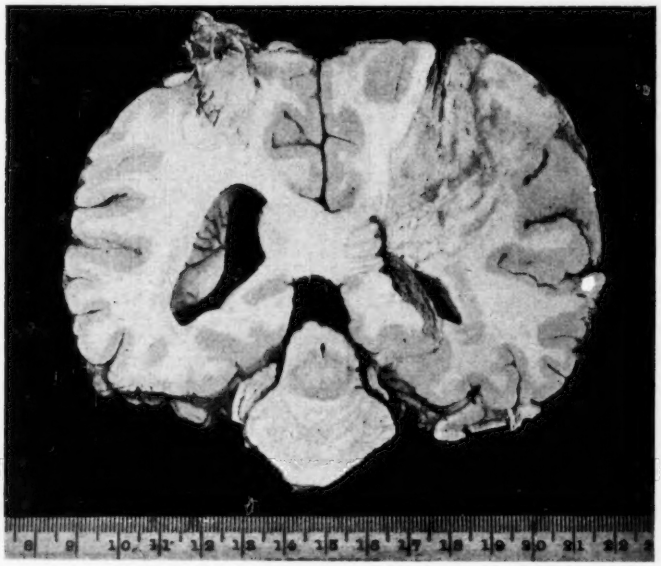


FIG. 1A.

and most of it undercut by tumour which finally ended in the white matter underlying the second occipital convolution. There were a few small nodules of growth in the posterior part of the superior temporal gyrus. Medially the tumour spread deeply into the hemisphere, destroying or cutting off most of the white matter of the parietal lobe, invading the occipital radiation of the corpus callosum and destroying the upper half of the sagittal strata so reaching the outer wall of the trigone of the lateral ventricle (fig. 1B). The right lateral ventricle was markedly depressed and distorted, the left dilated and the lenticular nucleus and posterior part of the right thalamus compressed. Otherwise the right thalamus appeared macroscopically normal. At the level of the splenium there was a small tumour in the upper extremity of the left postcentral gyrus, extending for about 2½ cm. down into white matter and 1 cm. sagittally fig. 1B).

The tumour in the right hemisphere proved to be a spongioblastoma multiforme. It was exceedingly vascular and there were large areas of hæmorrhage and necrosis, giving the growth its marble-like macroscopic appearance. The meninges were extensively involved on this side. The tumour in the left hemisphere, though

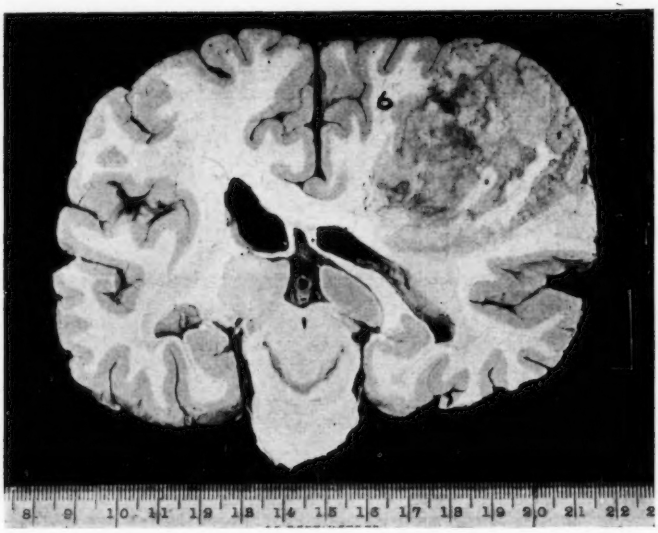


FIG. 1B.

also a spongioblastoma, was neither as hæmorrhagic nor as necrotic, and in some areas the appearances were those of a fibrillary astrocytoma. The meninges in the right hemisphere were extensively invaded by growth.

The thalamus was not studied in detail. Examination of some representative sections revealed no invasion of the right thalamus by tumour. Sections cut from celloidin blocks and stained with cresyl violet and Heidenhain showed a heavy outfall of cells in the posterior part of the right lateral nucleus and pulvinar, when compared with sections from the left side. There was also considerable gliosis here, and many of the remaining cells showed retrograde degeneration.

COMMENT ON CLINICAL FINDINGS IN CASE 1

In addition to the anosognosia and body image disturbance, with which we are chiefly concerned here, the clinical picture in this patient illustrated some other effects of lesions of the right parietal lobe. Among these were ocular deviation and rotation of the trunk to the right, visual disorientation, and apraxia for dressing. Her failure in constructional tests and confusion of planes in drawing suggested a disturbance of visual-spatial cognition, of the type described by Paterson and Zangwill (1944) in right parietal lobe lesions. (This was not studied in any detail.)

The visual disorientation is most satisfactorily accounted for by inattention to the left half of space, resulting in an almost mechanical preference for right turnings. Her behaviour offered confirmation for the explanation of this type of spatial disorientation suggested by Pötzl (1928) and amplified by Brain (1941). The defect was the spatial equivalent of the allæsthesia for sensory stimuli exhibited by this patient, for, as Brain

(1941) has pointed out, disruption of the scheme for one-half of the body causes stimuli applied to it to be related in consciousness to the intact scheme for the normal half and, similarly, "severe damage to the scheme for one-half of external space causes the remaining half to exert a dominant influence in the choice of routes."

By the time fixed delusions about the left side were present, together with bizarre confabulations to explain its weakness, the patient also had disorientation for time and space, retention defect, with an incongruously euphoric affect. This intellectual and affective disorder, especially the memory disturbance of Korsakoff type, almost certainly made its contribution to the picture of anosognosia. Some authors, Stengel (1944), Sandifer (1946), have laid special emphasis on the dementia and clouding of consciousness, holding that anosognosia for hemiplegia does not develop in their absence. There is no doubt that such delusional misinterpretations evolve more easily in this type of setting. However, it will be remembered that our patient's attitude to her paralysed left side, while not yet grossly deluded, was distinctly pathological at a time when she had no clouding of consciousness or other intellectual defect beyond some apathy, drowsiness and retardation. Our next case shows more explicitly that anosognosia is not simply dependant upon the intellectual disorders frequently associated with it.

The persistent neglect of her left side by this patient preceded the overt expression of any delusional ideas concerning her paralysis. This suggests that the disturbance of the body scheme was primary and determined the subsequent denial of the hemiplegia.

Case 2.—Male aged 51. On June 17, 1947, suddenly developed bilateral frontal headache and vomiting. Two days later he was admitted to a local hospital. He was observed to be irritable, irrational and disorientated. Lumbar puncture on June 19, 1947, produced blood-stained fluid under very high pressure. On June 24 he was thought to have papillœdema and was therefore transferred to the Atkinson-Morley Emergency Hospital under the care of Mr. Wylie McKissock. On admission here he was co-operative, correctly orientated, but his memory for recent and past events was impaired. He appeared to be hallucinated, had ideas of influence and paranoid delusions. He thought everyone considered him insane, but was convinced of his sanity. The "so-called X-rays" which had been taken were part of an organised scheme, with some sinister purpose.

The only positive findings on physical examination were B.P. 185/110 neck rigidity, early right papillœdema, and an increased right biceps-jerk. X-rays of skull normal. Blood urea 65 mg. E.E.G. within normal limits, C.S.F. findings: no xanthochromia, R.B.C. 20, W.B.C. 7, Protein 10 mg. Sugar present. W.R. negative. (2.7.47)

On 7.7.47 bilateral common carotid arteriography was performed by Mr. Kenneth Till. The vascular tree showed good filling on both sides and showed no abnormality. On July 18 he was sent back to his local hospital.

His headache, which had been present since commencement of the illness, continued unchanged. On August 5, 1947, he developed severe localized frontal

pain, radiating down the right side of his face and into the occipital region. There was also pain in the lower back, radiating down both legs up to the ankles, and he complained of diplopia. Right ptosis was observed. He gradually became confused and disorientated and finally lost consciousness. He was comatose for four hours. He then came round and his condition improved progressively until his readmission to the Atkinson-Morley Hospital on August 15, 1947.

On examination here he was alert and normally orientated. The positive findings on physical examination were: early papilloedema, a fixed right pupil with an almost total paralysis of the right 3rd nerve, and some inco-ordination of the right lower limb. Kernig's sign was positive. A diagnosis of aneurysm of the right internal carotid artery was made. Intermittent carotid compression was carried out between 19.8.47 and 12.9.47, when an arteriography was again performed. This showed a large aneurysm on the supraclinoid portion of the internal carotid (fig. 2A). The internal carotid was therefore ligated. He made an uneventful recovery and was discharged on 9.10.47.

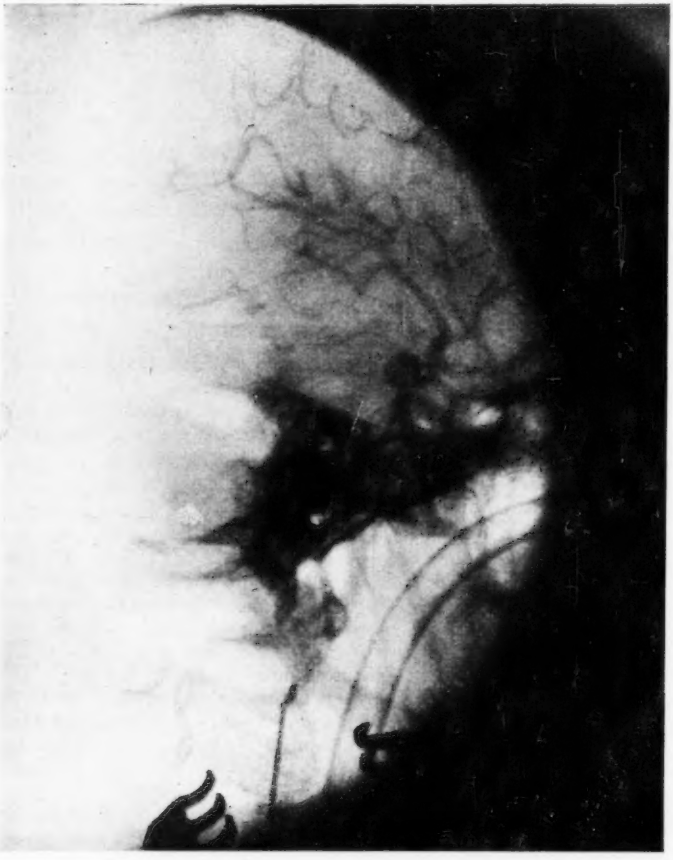


FIG. 2A.—Arrow indicates aneurysm on supraclinoid portion of internal carotid artery. It is instructive to note that the arteriogram taken two months previously (fig. 2B) showed no aneurysm. (By kind permission of Dr. J. W. D. Bull.)

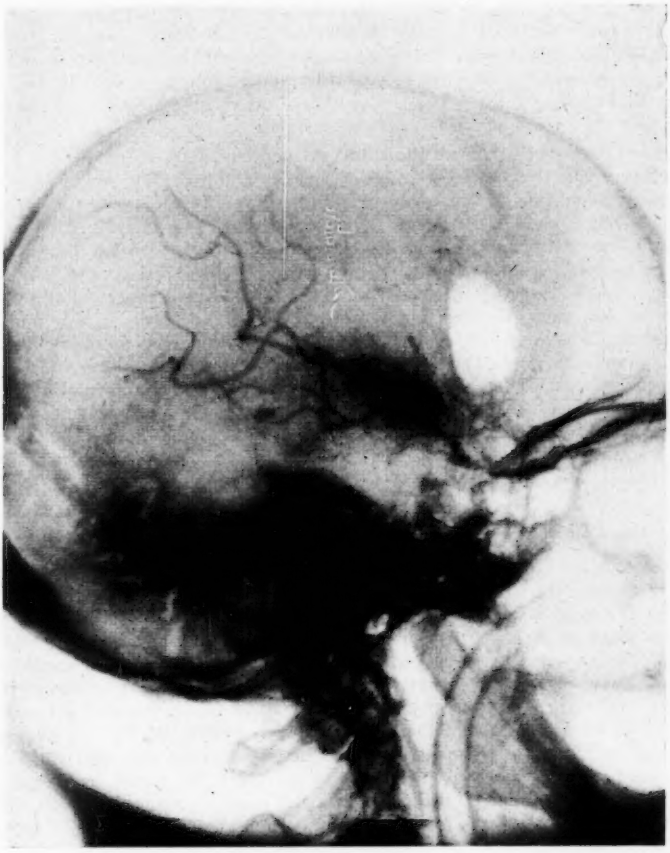


FIG. 2B.

The same evening he suddenly went pale and lost consciousness. According to his wife his legs carried out jerking movements. On recovering five minutes later he complained of severe headache over the right eye. After two days in bed he got up. Apart from headache he then remained well until 15.10.47, when he suddenly developed a left hemiplegia without losing consciousness. He was confused during the night and appeared very perplexed over his left arm, which he did not consider his own, asking his wife repeatedly if it belonged to her. He was readmitted to the Atkinson-Morley Hospital on 16.10.47.

On examination his memory for recent events was poor and he was disorientated for time, but he was otherwise in touch with his surroundings and able to co-operate on examination. The positive findings on physical examination were a complete homonymous hemianopia, total right 3rd and 4th cranial nerve palsies, complete left hemiplegia, with increased deep reflexes in the left lower limb and a left extensor plantar response. There was absence of all forms of sensation on the left side.

On 16.10.47 lumbar puncture produced clear fluid, pressure 200 mm. Examination showed R.B.C. 10, W.B.C. 5, protein 10 mg., so that no recent fresh hæmorrhage into the subarachnoid space could have occurred. An E.E.G. showed a widespread abnormality in the right hemisphere with suppression of the alpha rhythm and presence of medium voltage slow wages, ranging from 2 to 4 a second (Dr. G. B. Parsons-Smith). The abnormality was most marked in the temporal region, but also spread upwards towards the vertex.

During the week after readmission he showed marked emotional lability, fluctuating constantly between a fatuous jocularity and a readily evoked tearfulness. His mood was at times infectiously gay, and he would then make frequent jokes and puns, but a sudden change to a fit of weeping was likely at any moment. There was no spontaneous complaint of anything wrong with his left side. He was very restless in bed, and, as his eyes were kept deviated to the left and he tended to ignore the left half of space, he was in constant danger of falling out of bed on the left side. During this week there was frequent bouts of agitated and importunate behaviour, in which he wept and complained bitterly there was another man's arm in bed with him. He could usually be calmed, and, with his eyes open, persuaded that the arm was in fact his own. However, with his eyes closed he would insist it was the examiner's, even when made to trace it to the shoulder with his healthy hand. He seemed totally unaware of his paralysis, but complained repeatedly about his right ptosis, often showing great distress as he did so.

On 24.10.47 it was observed that he had difficulty in naming his fingers, and a more detailed psychological examination was carried out.

His attention was easily aroused, but he was distractible, commenting on irrelevant events occurring round him. His memory for remote events was good, while for the various stages of his illness it was hazy, owing probably to his having at times been in a state of clouded consciousness. However, he remembered some of his experiences in states of confusion. Thus he could recall during his first illness in June 1947 hearing voices shouting threats and abuse at him, orderlies and nurses plotting against his life, &c. His retrospective insight was good and he described these hallucinations and delusions as "due to my imagination worked on by illness." He was also aware that his emotions were abnormally labile and unpredictable. His concentration and retention, as tested by simple tests, were good. He repeated stories accurately and reproduced seven numbers forwards and five backwards. He was fully orientated for person, time and place. There was a slight disorder of time perception—time had appeared to him to pass very quickly since his last illness had commenced, and this was confirmed by his judging the passage of twenty minutes as ten. His general information was excellent.

Other psychological findings were as follows:

Body image disturbance.—On October 24 he was still unaware of his paralysis. Asked to raise his left arm or leg, he would raise the right instead. If his mistake was pointed out he would look perplexed, but make no comment. Asked if there was not something wrong with his left side, his reply on one occasion was "Well, no one has told me there was anything wrong with it." No further attempt was made to convince him of his paralysis. Although he often seemed in doubt when the subject was first raised, he could now be persuaded on each occasion that the left arm and leg were in fact his own. In spite of this verbal rationality, which

could now be evoked on each occasion the ownership of his left limbs was discussed, the impression was still that there was an underlying idea carrying delusional force against all evidence to the contrary, that the left upper and lower limbs were in some way foreign to him. He complained repeatedly that his arm pressed down on his body, causing him pain, and asked to have it "moved out of sight." Strangely, the delusion did not extend to the trunk or face. He remained anxiously concerned about his left ptosis to the complete exclusion of any concern about his hemiplegia.

He was able to point to eyes, nose, shoulder, and name them without difficulty. He was, however, unsuccessful in naming or demonstrating his fingers. On the left side he was nearly always wrong in naming the middle three fingers and made frequent mistakes in naming his thumb and little finger. On the right side he had less difficulty, but often hesitated before attempting to show the finger named, and made repeated mistakes in naming and demonstrating the index, ring and middle fingers. He made mistakes in naming thumb and little finger also, but less often than for the left hand. When asked to point to a finger on the left hand corresponding to one touched by the examiner on the right, while patient's eyes were closed, he seemed completely at a loss and pointed to fingers at random. If touched on the right hand with his eyes open, he could point to the corresponding finger on the left. Imitation of finger movements with the right hand was grossly incorrect. The thumb seemed to be more successful than other fingers in imitating movements. He made repeated mistakes in identifying fingers on both of the examiner's hands, but correctly named other parts of his body. To throw light on the finger agnosia he was confronted with two sets of five matchsticks and asked to pick out individual ones named by number (Stengel, 1944)—nearly all his efforts were correct. With sticks of different sizes he was equally successful. He was also given a test suggested by Brain (1941). He was pricked on the right hand and asked to indicate the spot on a diagram of the hand. He could do this correctly if he was allowed to see the spot touched, but not if his eyes were closed. Since there was no disturbance of superficial sensation on the right hand, this could only be explained as due to his inability to relate the stimulus to a scheme of his hand.

Spatial orientation.—There was a tendency to underestimate distances within "leg reach," but answers were never more than one-third of the distance out. Relative localization was normal.

He hesitated a great deal when asked to show left and right sides of his body, especially when naming his limbs. However, he corrected all his mistakes and, as he was able to point to examiner's right and left sides with less difficulty, there was no real right-left disorientation. He was able

to judge which of two lines was longer or which of two objects was nearer to him. Judgment of relative length of lines was not dependent on their being parallel to each other.

Clock tests.—The patient mistakenly placed the minute hand on the right side instead of the left very frequently. There were no mistakes in placing the hour hand. The former defect is probably due to allæsthesia (Paterson and Zangwill, 1944).

Visual constructive disabilities.—Visual perception: There were no difficulties in identifying pictures or in naming incongruous features. Interpretation of pictures on the Stanford-Binet Scale was on a normal adult level, but he had to study the pictures for a long time on account of his defective vision.

Examination for apraxia: There was no difficulty in carrying out actions to order. He was both able to identify objects, use them correctly, and represent their use without seeing them. Thus, he could button up his coat with his right hand, write with pen or pencil, cut with scissors, as well as beckon, salute, pretend to smoke a cigarette, or to use a key in a lock.

Constructional tests.—Very simple geometrical figures with bricks or matches were reproduced in a recognizable sort of manner. He was agile and accurate in using his right hand. In attempting more complicated patterns he showed a very marked defect. He seemed to set about it in the correct way, choosing the right number of bricks or matches for parts, but in articulating them seemed to become confused. All the parts could be distinguished in the final pattern, but their arrangement was incoherent. There was a tendency to crowd matches into the right half of patterns and to leave the left side incomplete. He was quite unable to get beyond the first three patterns on Koh's block series, in spite of repeated explanation and encouragement. He seemed unable to grasp that one side which was half-blue and half-yellow would provide him with the necessary pattern. (There was no doubt that this represented a very gross deterioration on former performance. His I.Q. on the Wachsler Bellevue Verbal Scale was 131. Furthermore, although he was using only one half-field in these tests, his visual acuity was between 6/6 and 6/9 in this left eye.)

In copying and drawing, simple geometrical patterns were easily reproduced, but difficult ones were copied with gross errors. Drawings of common objects showed anomalous features. Parts tended to be disproportionate and their planes confused. Thus, a bicycle was drawn in side view, but the front wheel shown end on. In his first attempt the front wheel (which was on the left of the drawing) was completely omitted. A disproportionately small wheel was added as an afterthought, after hints had been dropped that parts were missing. In drawing a bus,

the back wheels were omitted. The anomalies were not due to lack of artistic skill. There was no difficulty in connecting dots with a straight line, in stating whether objects were above or below a line. He drew arrows pointing upwards and downwards correctly.

Writing and reading: No difficulty in writing or spelling. In reading the patient often lost his place as a result of missing one or two lines.

Counting and calculating were normal. The patient was able to give correctly the number of objects presented to him, provided these were placed close together.

Sorting tests: There was no difficulty in sorting objects according to colour, use, shape or size.

Plan drawing: In attempting a ground plan of the ward he showed the characteristic defect described by Paterson (1944). The approach to this problem was piecemeal—separate parts of the plan being put down in a disconnected manner without apparent reference to the whole conception. The final result was fragmented and inaccurate. The left side of the rectangle representing the ground plan of the ward was omitted.

Progress

After about October 28 he began to pay more attention to his left side, and within the course of the next few days he developed full knowledge of his disability and insight into his former delusions. The excessive concern with his ptosis disappeared. On November 2 he was able to name and identify his fingers with little hesitation, correcting occasional mistakes without prompting.

He was discharged from the Atkinson-Morley Hospital on 11.11.47. A letter from his doctor on January 30, 1948 (in answer to a follow-up note), stated that his physical condition had undergone no change, but he was mentally clear, emotionally equable and calm and able to identify all parts of his body without confusion or hesitation.

Comment on Case 2

The development of the left hemiplegia and hemianæsthesia four weeks after ligature of the right internal carotid was difficult to explain, in view of the normal C.S.F. As the onset was sudden, the cause was presumably a vascular catastrophe. One possible explanation was a large intracerebral leak from the aneurysm into the right hemisphere. Richardson and Hyland (1941) have stressed the frequency with which intracerebral hæmorrhage occurs in intracranial aneurysm, sometimes without hæmorrhage into the subarachnoid space.

The delusional attitude towards the left side of the body appeared in a setting of clouded consciousness, which doubtless facilitated its initial

development. However, the patient remained deluded for two weeks, during most of which he was in normal contact with his surroundings, his only intellectual defect in this period being a patchy amnesia for recent events. Like the first case, therefore, this case suggests that anosognosia for hemiplegia may occur in the absence of dementia or clouding of consciousness due to generalized cerebral disease.[1]

The homonymous hemianopia and right ocular palsy make it difficult to draw any definite conclusions about the patient's visual-spatial disabilities. However, in view of the characteristic disarticulation and incoherence of his reproductions in constructional tests and drawings, &c., it is highly probable that constructional apraxia was, in fact, present in this case.

Finger agnosia is nearly always produced by a lesion of the left hemisphere. The only other case on record, as far as we are aware, in which both finger agnosia and agnostic disorder for the left half of the body were caused by a lesion of the right hemisphere, is that described by Hermann and Pötzl (1926). Their patient was an ambidexter. Our patient gave a history of left-handedness in several cousins. Although the possibility of a lesion in the left hemisphere of this case cannot be excluded with certainty, in view of the absence of any signs or symptoms to suggest it, it is sufficiently remote to be ignored for practical purposes. As in Hermann and Pötzl's case, the probability in this patient was that the right hemisphere was dominant, the transfer of dominance having caused it to assume the function of both major and minor hemispheres for representation of the body image.

The patient was able to select any one of five sticks of equal or different sizes without difficulty, but unable to select fingers correctly, showing that finger agnosia was not just an inability to select one of several objects. His performance in the test devised by Brain and his ability to name other parts of his own and the examiner's body were in accord with Gerstmann's view that the condition is an isolated form of autotopagnosia. Brain (1941) reached the same conclusion from a study of a boy of 15 with a left hemisphere lesion.

There was no acalculia, agraphia or definite right-left disorientation, all of which are often associated with finger agnosia in the Gerstmann syndrome. The incompleteness of the syndrome in this case was not by

[1]We must qualify this statement by pointing out that experiences during the initial stage of confusion in this second case may have played a part in the subsequent perpetuation of the delusional attitude in clear consciousness. If so the anosognosia would have been akin to the "residual delusion" after delirium described by German writers. The possibility that such prior, transient delirious episodes have played some part when anosognosia for hemiplegia is seen without general intellectual disturbances requires investigation.

any means unique. Though not generally appreciated, it is yet an undoubted fact that any of its typical constituents may be absent from Gerstmann's syndrome. It has been described without agraphia (Mayer-Gross, 1936), with little or no acalculia (Lange, 1930; and Mayer-Gross, 1936) and without finger agnosia or right-left disturbances (Mayer-Gross, 1936). In one of Guttmann's cases, acalculia was associated only with constructional apraxia, and this was added subsequently to the isolated arithmetical defect. Finger agnosia may recover, leaving acalculia undisturbed (Guttmann, 1936), while agraphia, constructional apraxia and acalculia have each been described independently. It is difficult to reconcile these facts with attempts that have been made to relate the complex of symptoms in Gerstmann's syndrome to a single psychological defect, such as impairment in spatial perception. They clearly point to the relative independence of each of the symptoms.

Although the facts do not permit of factors of a fundamental determinative kind, there is no doubt that certain psychological factors are shared in common by the separate components. To some extent these are created secondarily by the mutual interplay of those components present in any given case. Thus, Mayer-Gross and Guttmann (1936) have shown how constructional disturbances may influence, though they do not determine, acalculia or the figure writing defect, and we can understand how the acalculia in Stengel's patient would, in his attempts to pick one of several objects, create difficulties which did not exist in our patient. It follows that the psychological basis of finger agnosia is not necessarily the same in each case, and this may partially account for the inconsistencies in the findings of different authors. This requires confirmation by the investigation of more cases of finger agnosia.

Discussion

In our present state of ignorance about the mode of evolution and physiology of the body image, no complete explanation of phenomena such as anosognosia for hemiplegia are possible. It is evident that the condition cannot be accounted for in terms of the sensory loss which is usually present, and the importance of which has been emphasized in some explanations put forward (Barré, 1923; Barkman, 1925). The patient usually retains adequate sensory and intellectual means for discovering his hemiplegia. The remarkable thing is that he ignores the evidence that confronts him and, when this is presented to him, rejects it in favour of a delusion. Cortical hemianæsthesia in association with hemiplegia is relatively common, but anosognosia for hemiplegia is rare. Strange subjective experiences are often reported by hemiplegic patients with severe sensory impairment on the paralysed side, but their attitude is one of

anxious preoccupation with the affected body half and not, as in anosognosia, neglect of it and ocular deviation to the opposite side. When a patient ignores part of his body, his condition is no longer accountable in terms of sensory loss alone. For such behaviour is delusional, whether or not he expresses delusional ideas, and must be based on a defect of an agnostic kind.

Among explanations of a psychological kind the best known is that of Schilder (1935) who suggested that anosognosia was an "organic repression," that is, the result of a process similar to psychic repression in a psycho-analytic sense but due to organic factors. But repression is a metaphoric description of a psychological phenomenon, the physio-anatomical basis of which is unknown. This explanation therefore fails to throw much light on the disorder.

Affective factors often play some rôle. Thus, the affective pressure against the acceptance of disease doubtless played a part in the "displacement" of all anxiety and distress from the grave disability consti tuted by his hemiplegia in Case 2, to the trivial one produced by his ocular palsy. Likewise, the fatuous euphoric affect exhibited by Case 1, and present less consistently in Case 2 made its contribution to the delusional state in each. However, such factors can only play a subsidiary rôle in colouring the clinical picture and influencing its content.

Although the anosognosia in our two cases could not be attributed to dementia or clouding of consciousness, these are frequently recorded as being present throughout the period in which the disorder is manifested. In such cases the intellectual disturbances probably play an important part in facilitating the delusional state by causing constriction of the perceptual field and defective retention of recent impressions. The more extravagant anosognostic delusions have been mostly described in a setting of generalized cerebral disorder, such as delirium. Examination of the difference in the course of our two cases offers a suggestion that this may have been determined by the opposite trends pursued by the general intellectual disturbance in each. In the second case the subsidence of the delirious state was followed after a time-interval by acceptance of the hemiplegia and the development of full insight into the delusions previously held, although the left-sided sensory loss and his other physical defects remained unchanged. In the first case, however, there was progressive mental deterioration and the delusional attitude towards the hemiplegia continued until death. One rôle of the general intellectual disturbances, when present, may therefore be to prevent the re-creation of the body image and the patient's adjustment to his paralysis which tend gradually to occur after a time lag in their absence. These and other points require elucidation by detailed investigation of intelligence, orientation, memory,

retention and concentration, and other psychological functions, in all cases of anosognosia, as well as the temporal relationship of the defects present to the delusions about the body.

In any individual case the total picture of anosognosia for hemiplegia is doubtless determined by a constellation and interplay of factors such as changed subjective experience of the body due to sensory loss, agnosia for the left half of space, ocular deviation to the right, and often generalized intellectual disturbances and emotional dissociation.

However, it becomes especially apparent where there is little or no generalized intellectual disturbance, that it is difficult to account for the syndrome without postulating an additional and possibly fundamental factor of agnosia for the body, in consequence of which the patient's orientation with respect to his body, is disturbed in a specific way, and he is no longer able to relate himself to it correctly.

Even confused and demented people do not always deny a painless hemiplegia, and it would seem reasonable to assume that a specific, focal disorder of cognition, arising from a disorganization of the body scheme, makes its contribution to the genesis of the disorder in all cases.

It is difficult to believe that the two components of agnosia for the body half and unawareness of disease in it are independent and not causally interlinked. It has even been suggested that they are due to separate lesions in the parietal cortex and thalamus respectively (Nielsen, 1938), but the inconsistencies in this theory have been pointed out by Sandifer (1946). Both our cases, in common with the majority of those published, ignored the left half of their bodies. Moreover in our first case, as well as two other cases we have observed more recently, behaviour expressive of estrangement from the hemiplegic side was observed before delusions about the paralysis were expressed. Our experience leads us to suspect that the derangement of the body scheme underlies and determines the denial of paralysis. The attitude to the disability is not, of course, precisely the same in each case being determined in detail by the contingencies of the individual personality and constitution.

The neurological lesions in anosognosia for hemiplegia.—There is a great deal of evidence to suggest that this type of body image disorder is produced by a lesion of the right parietal lobe (Pick, 1896; Pötzl, 1925; Barkman, 1925; Hagen and Ives, 1937; Gerstmann, 1942). Such a lesion has been a constant finding in all cases of anosognosia for left hemiplegia examined post mortem, even when the syndrome has been manifested in a setting of mental confusion. It has been suggested (Sandifer, 1946) that anosognosia for hemiplegia may result from lesions at any level, provided an accompanying intellectual defect is present. While this is probably true with respect to anosognosia for blindness, there is no positive evidence

in its favour as far as anosognosia for hemiplegia is concerned. The available facts may be more economically accounted for by the assumption that a lesion or disordered function of the right parietal lobe is present in every case, and that such a lesion is specific for that part of a confusional state which consists of, or is an elaboration upon, an agnosia for the left half of the body.

In our first case a massive lesion of the right parietal lobe was demonstrated post mortem. The small neoplasm in the left parietal lobe was probably irrelevant to the anosognosia. In the second case the physical and psychological findings were suggestive of an extensive fronto-parietal lesion.

The part of the parietal lobe specially concerned with the body image is not definitely known. Since sensory loss cannot by itself cause anosognosia, a lesion of the somatosensory projection on the post-central gyrus alone cannot account for the syndrome. A number of facts point to the region of the right supramarginal and angular gyri as the possible site of the essential lesion. The ocular deviation to the right seen in both our cases in common with the great majority of recorded examples of anosognosia receives a simple explanation from the involvement of the angular gyrus (Fulton, 1943). A consideration of certain anatomical facts is germane here. The supramarginal and angular gyri receive the projection of the pulvinar of the thalamus. The pulvinar is connected with the lateral nuclear mass, the geniculate bodies, and also receives in primates a large projection from nucleus ventralis posterior. Its cortical projection is in more than one plane, so that the supramarginal and angular gyri receive highly elaborated sensory impulses (Walker, 1938). The complex thalamo-cortical unit thus constituted is probably concerned in the integration of different sense data in highly specialized functions, such as stereognosis. It is also well equipped anatomically to effect the necessary integration from its somato-sensory, visual and vestibular components of the body image. The accurate delimitation and detailed differentiation of the body is a function peculiar to man and the basis of some of his highest skill. This may be one reason for the growth and differentiation of the supramarginal and angular gyri in the course of phylogenesis proceeding *pari passu* with a progressive enlargement of the pulvinar.

Pötzl's contention (1925) that anosognosia for hemiplegia was due to the coincidence of lesions in the parietal lobe and thalamus of the minor hemisphere was not borne out by subsequent reports which showed that a lesion of the right parietal lobe was adequate by itself to give rise to the condition.

In our own case the right thalamus was compressed, but otherwise macroscopically normal. The changes observed microscopically were

almost certainly secondary to pressure and destruction of the thalamo-cortical projection by tumour.

On the other hand, there is a certain amount of evidence to suggest that lesions of the thalamus alone or of the thalamo-parietal peduncle, isolating it from the cortex, may cause the syndrome (Barkman, 1925; Van Hagen and Ives, 1937; Nielsen, 1938). The part of the thalamus responsible for the disorder has not been investigated, but it is noteworthy in this connexion that the known clinical syndromes produced by vascular lesions of the thalamus have never been recorded in association with disturbance of the body image. Either the whole thalamus must be destroyed, therefore, for such a disturbance to appear (and this does not seem to have occurred in the published cases) or, what is more likely, the lesion must be at a special locus within the thalamus to produce it. In view of what has been said above it would be instructive to determine whether or not the pulvinar is commonly involved in disorders of the body image seemingly caused by a thalamic lesion alone. (It is surprising that almost nothing is known about the clinical effects of lesions of the pulvinar, a thalamic nucleus which has become increasingly prominent in the course of evolution.)

The body image and the major hemisphere.—There is some doubt about the types of body image disorders that may be produced by lesions of the major parietal lobe. By far the commonest condition is finger agnosia, usually with other components of the syndrome described by Gerstmann. The lesion responsible for this syndrome is said to be situated in the angle between the posterior part of the angular gyrus and the second occipital convolution (Nielsen, 1938).

The combination of finger agnosia with anosognosia for right hemiplegia is very rare. The only other example which has been recorded, to our knowledge, is the case of Hermann and Pötzl (1926) who was an ambidexter. A transfer of dominance to the right hemisphere was likewise the probable explanation in our case (*vide supra*).

Brain (1945) has suggested that lesions of the left parietal lobe, like those on the opposite side, produce an agnosia for the contralateral body half, which is obscured by the associated intellectual defects. Gerstmann's view is that finger agnosia is a localized or incomplete autotopagnosia, and that gross lesions of the major hemisphere may produce a total autotopagnosia or inability to name any part of the body. Although it is doubtful if the latter exists outside a picture of confusion, dementia or clouded consciousness, there is some evidence that a lesion of the left parietal lobe is necessary before it can be manifested even within such a setting.

In a case of total autotopagnosia published by Nielsen and Ives (1938) there were several lesions in the brain, but by far the largest was in the

left angular gyrus. Another case of Nielson and Sult (1939) commenced with a mental confusion and sensory aphasia which subsided and were followed by total autotopagnosia. This in turn narrowed to the picture of Gerstmann's syndrome. In a case described by Gerstmann (1942) the vascular lesions clinically appeared to be confined to the left hemisphere.

There tends to be some association between disorders of the body image and disturbance of praxis and spatial perception. Thus finger agnosia, apraxia in finger demonstration and a gnostic disturbance for the "activity space" of the hands tend to occur together while agnosia for the left body half is commonly accompanied by agnosia for the left half of space. Apraxia when due to a left parietal lesion is bilateral, but affects the left hand only when caused by a right-sided lesion. As in addition visual disorientation when produced by a left-sided lesion commonly affects both halves of space (cf. the visual-spatial disorders in constructional apraxia, right-left disorientation and, according to Nielsen, loss of topographical memory),[1] there would appear to be some grounds for supposing that at the level of gnostic and practic functions the left hemisphere is predominantly concerned with both sides of the body and its dispositions in both halves of space. It would not be totally unexpected, therefore, if a left parietal lesion were concerned as Gerstmann suggests in the production of a total autotopagnosia.

Whether this condition or an agnosia for the left body half is the product of such a lesion remains to be tested by a detailed analysis of actual cases. The associated aphasic and intellectual disturbances are not always so severe as to preclude this in every case.

The vulnerability of the left body half and the fingers.—It is clear that certain parts of the body image are specially vulnerable, as shown by the marked frequency of agnosia confined to the left body half and the fingers, while agnosia for other parts of the body is almost unknown. The cause for this is not clear, but the available facts about the genesis of the body image and its rôle in motility suggests a possible explanation. The body image comes to be defined as a result of perception of stimuli originating from its cutaneous boundaries and experience of its constituent parts in movement. According to Schilder pain plays an important part in this definition of the body. In lower animals a poorly developed pain sense seems to be associated with a crude differentiation between body and external world. Thus, a dragon-fly feeds on its own body when its rear end is placed between its jaws (Uexküll, 1927). Even in higher animals

[1]The one established exception appears to be defective localization in the opposite homonymous half-field which may be produced by a left or right parietal lesion (Brain, 1941).

this differentiation is on a primitive level, for a rat tends to eat its deafferented fore-limb.

However, in man the formation of the body scheme is effected, to a large extent, by the recording of perpetual changes in position. Skill in purposeful movements depends on the completeness and differentiation of the ever-changing schema thus constructed, and this is in turn enriched by each new alteration in the body's outline. The most highly skilled activities, namely those executed by the fingers, are acquired last. It is of interest in this connexion that differentiation of the fingers is achieved comparatively late in children (Freeman).

In the evolution of all highly skilled activities, such as writing, playing the piano, &c., there are two stages. In the first there is a consciously directed visual control of the movements performed by hands and fingers. In the second, the newly acquired movements become gradually automatized and figure less and less in consciousness on performance. The more complex the automatization, the greater the mastery. Should conscious awareness of the movements reappear on account of disease, a decrease of efficiency is the result. This does not only apply for the hands, although it is the latter which are called upon to perform most of the activities that proceed in this way from a more conscious to a more automatic stage.

Another factor that determines skill is strong dominance of one hemisphere (Riddoch, 1941). This predominance of the right or master hand inevitably involves comparative oblivion for the opposite hand. As Schilder has pointed out, there is a normal tendency to forget the left side of the body. The secondary automatization of skilled movements described above demands a similar forgetting of the hands. Both types of "somatamnesia" must be based on some physiological process. It seems likely that the special vulnerability of the left side of the body and the hands is connected with the fact that each individual learns partially to exclude them from participation in the conscious processes that accompany certain volitional activities.

Anosognosia and depersonalization.—Comparisons have been rather loosely drawn between anosognosia for hemiplegia and the psychiatric disorder known as depersonalization. However it is necessary to be precise about what one is comparing, if light is to be shed on both types of disorder from the comparison. In anosognosia there is a delusional state of a psychotic kind, often with a flattening or even incongruity of affect. Depersonalization, on the other hand, may be described as a neurotic reaction to unpleasant subjective experiences. Affect is usually congruous and insight is retained. Furthermore, depersonalization of hemiplegic distribution has not been described.

There are, however, interesting similarities which deserve further investigation. Many features of depersonalization suggest an important organic element in its causation. Among these are the sudden onset, often with the experience of "something snapping in the head." A satisfactory psychogenetic explanation of the disorder is frequently lacking. Associated with the changed bodily feelings are impairment of spontaneity of thought, movement and affect, and its replacement by persistent self-awareness hindering thought and volition and blunting emotion. The introspective descriptions of these patients lend themselves to the interpretation that secondary automatization of function has been lost, with regression to a more primitive level of self-conscious experience. This suggestion of an impairment in some fundamental physiological mechanism is further supported by the fact that experience very similar to those in depersonalization may be artificially produced by mescaline.[1] It will be evident that anosognosia and depersonalization are in that fascinating borderland between neurology and psychiatry, the exploration of which will probably shed light on important problems of both subjects.

SUMMARY

(1) Two cases of anosognosia for hemiplegia are described. One case was associated with a partial Gerstmann syndrome. The findings in this case were consistent with Gerstmann's explanation of finger agnosia as a localized form of complete autotopagnosia.

(2) In neither of the two cases reported here were generalized intellectual defects present throughout the period of delusional behaviour with respect to the left body half. The factors contributing towards the production of anosognosia for hemiplegia are critically considered. It is argued that a disorder of the body scheme underlies the denial of hemiplegia, and that this is independent of the generalized intellectual disturbances which are often though not invariably present.

(2) The post-mortem findings in the brain of one case are described. The possible site of the lesions necessary to produce anosognosia for hemiplegia are discussed.

(4) The vulnerability of the left half of the body and the fingers for becoming involved in gnostic disorders is discussed, and possible reasons for this suggested.

(5) Some points of similarity between anosognosia for hemiplegia and the syndrome of depersonalization are considered.

[1]Cf. Guttmann (1936). "There were funny sensations in my right hand. If I looked at it and observed its normal shape I had nevertheless the feeling that it was huge and inseparable from surrounding space." *See also* Brain (1947).

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Notices of Recent Publications

Atlas of Neuropathology. By W. Blackwood, T. C. Dodds and J. C. Somerville. 1948. Pp. 212. With 262 illustrations, some in colour. Edinburgh: E. & S. Livingstone Ltd. Price 35s.

Although pathology, in so far as it is concerned with morphology, cannot be taught without illustration, questions of cost limit the illustrations in the average textbook to a minimum. An atlas in which the emphasis is placed on photographs and diagrams therefore fills a gap. In the present volume this method is used to present the most important facts of pathology in its relation to clinical neurology. In the condensed letterpress the senior author has managed to convey a large amount of information in a minimum of space, and although a certain degree of dogmatism is inseparable from this technique there are few statements with which the reader will cavil and several points are made which books on neuropathology generally miss. Naked-eye appearances are well illustrated, as well as those seen under the microscope and the coloured photographs of the external appearances of the brain deserve special mention. The illustrations of the vascular pattern of disease, as shown by Pickworth's staining technique, are a novel and valuable feature of the book. This aspect of pathology, with its functional implications, deserves fuller study especially in an organ which is so vulnerable to anoxia as the central nervous system. The diagrammatic line drawings used to convey the authors' teaching are also very useful. The numerous coloured photomicrographs are almost without exception excellent, but some of the half-tone monochrome prints would gain by greater contrast. Authors and publishers alike are to be congratulated on both the conception and the production of a book which conveys in an attractive and easily assimilable form the essential elements of neuropathology.

Intracranial Tumours. By Percival Bailey. Second Edition. Oxford: Thomas, Springfield, and Blackwell Publications. Price 55s.

The second edition of this book will be warmly welcomed. It is a wholly admirable work alike in substance and in manner, Its author has paid his readers the compliment, not so usual as it once was, of writing in clear and dignified English. He has also had the courage to forsake the photograph for the drawing, and those he provides are excellent.

The descriptive clinical matter is of the highest order, while the pathology is what we have learned to expect from its distinguished author.

The book is one that should be in every neurologist's library.

The Metabolic Brain Diseases and their Treatment in Military and Civilian Practice. By G. Tayleur Stockings. 1947. Pp. viii + 262. With three illustrations. London. Baillière, Tindall and Cox. Price 16s.

The author presents a new classification of mental disorders (psychoses) into "dysoxic" and "dysglycic" types, either type being primary or secondary. Among the primary dysogias are simple and catatonic schizophrenia, depressive phases of the manic-depressive psychosis, certain paranoid disorders, derealization syndromes, obsessional states. Among the primary dysglycias are hebephrenic and paranoid schizophrenia and manic states. This classification has been suggested by the response of these conditions either to anoxia as in convulsion therapies, or to hypoglycæmia. It is supported by observations which suggest a disorder of cerebral metabolism as the cause of illness. The author has, in fact, constructed a new theory of the ætiology of the psychoses. This theory is based on a minimum of established fact and a maximum of gratuitous assumption. It ignores a large amount of accepted knowledge, such as that for instance which connects catatonic and paranoid schizophrenic states as aspects of the same disorder. Regarded from the centre of current psychiatric opinion, the author's views are eccentric in the extreme.